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SOME NEUROLOGICAL OBSERVATIONS IN 150 LAMINECTOMIES FOR SPINAL DISEASE AND INJURY.[1]

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During the past six years I have had the occasion to make a number of observations upon 150 patients with diseases or injuries of the spinal cord who were subjected to surgical interference. Some of the observations are here recorded, so that others may check up our results and report upon their own experiences.

Root Pains in Spinal Disease. Pearce Bailey and Joseph Collins have recently published papers in which they point out that frequently extramedullary spinal disease has, contrary to the general opinion, a painless beginning, while intramedullary disease may be characterized by the early appearance of root pains. Many of the cases reported by these authors were operated upon by the writer, and very often the operative findings gave the explanation for the presence or the absence of early root pains.

Thus we have found that in extramedullary tumors which develop under a slip of the dentate ligament, root pains are often missed among the early symptoms. The explanation for this is to be found in the anatomical relations between the dentate ligament and the posterior roots. The ligament lies in front of the posterior

[1] Read at the Meeting of the Section for Nervous and Mental Diseases, New York Academy of Medicine, October 10, 1916.

roots, and it is easy to understand that the latter are, to a considerable degree, protected against pressure from in front by the interposed dentate ligament.

We have made the interesting observation that large tumors are softer in consistency than the small ones, and are less apt to cause marked cord symptoms until the growth has attained a very large size. The small tumors, on the other hand, are often very hard, and rapidly exert considerable pressure upon the cord. Some of the large soft tumors do not cause pressure upon the nerve roots for a long time, and in cases of this kind, root pains as early symptoms are often wanting. In the large soft growths which surround the roots of the cauda equina (giant endotheliomas) early root pains are likewise relatively infrequent. It is surprising how little pain is complained of by a patient in whom the lower end of the spinal canal is filled with soft tumor growth which surrounds and envelops all of the nerves of the cauda equina.

I have operated upon several patients with small extramedullary growths on the posterior surface of the cord, who gave no history of pain as an early symptom of their disease. In these patients the tumor lay in the mid line of the cord on its posterior surface and had not attained a sufficient size to compress the origins of the posterior roots on either side. It is well known that excepting for the lines of attachment of the posterior roots, the spinal cord is not sensitive to pain, and the explanation for the painless early course in some patients with small extramedullary new growths is to be found in this insensitiveness of the cord tissue.

In intramedullary spinal tumors, on the other hand, early root pains do occur, and we have seen and operated upon two patients in whom the localized swelling of the cord from the growth occurred under a posterior root, so that the root was stretched very early and root pains were complained of among the earliest symptoms of the disease.

I do not wish to be understood as denying that early root pain is most frequent in extramedullary tumors and is relatively rare in intramedullary new growths, but the exceptions to this rule are so numerous, that one can not rely upon this symptom alone to differentiate between diseases which begin outside of or within the cord tissue.

THE SENSORY SYMPTOMS IN SPINAL NEW GROWTHS. In the majority of instances, a spinal disease which causes spastic paraplegia without any disturbance of sensation, is to be classed as a degenerative process in the motor pathways of the cord, but frequent exceptions to this rule occur. For example, I have operated upon a young woman and removed a large soft glioma which lay in the median line on the posterior surface of the cord in the upper dorsal region, in whom repeated careful examinations by experienced neurologists failed for many months, to find any sensory disturbance

at all. The history of this patient is of sufficient interest to report in detail:

Large extramedullary tumor of cervical cord; laminectomy and removal; cure.

Annie R., aged nineteen years, admitted to the surgical service of Dr. Sachs, at Mt. Sinai Hospital, on May 16, 1913. The patient had been seen for a number of months by Dr. Abrahamson, because of the complaint of a feeling of weakness in both lower limbs. Examination showed that the lower limbs were somewhat weak and that the knee and ankle-jerks were slightly exaggerated. There were no sensory disturbances of any kind. Three months before admission, the patient fell to the ground and when she was picked up, she found that her right leg was much weaker than her left leg. From this time on the weakness grew gradually more marked and the right leg became increasingly stiff. The left leg has also become somewhat stiff and weak. Since her fall, the patient has had urgency of urination with occasional loss of control of the vesical sphincter.

Physical Examination on Admission. The patient was a healthy looking young woman. Cranial nerves normal. Power in upper limbs good; reflexes not exaggerated; equal on both sides. Abdominal reflexes were present and equal. Power in lower limbs poor, but the right is much weaker than the left. Both limbs were very spastic. Knee-jerks exaggerated, right greater than left; ankle-jerks exaggerated, bilateral ankle clonus and Babinski. Wassermann and roentgen ray negative. Careful examination failed to reveal a disturbance of sensation in any part of the body.

May 18. A lumbar puncture was done and 6 c.c. of clear yellow fluid not under increased pressure were removed. After the spinal puncture, the patient began to complain of pain in the right shoulder.

May 20. Today, for the first time, there is some diminution in pain and temperature sensation up to the level of the second dorsal area, most marked on the left side. Tactile sensation is normal all over the body.

May 21. There is now complete loss of pain and temperature sensation up to the second dorsal level, but light touch is distinctly felt over the affected areas. Deep muscle sense is also not affected.

May 22. Today, for the first time, there is some diminution of tactile sensation below the area of distribution of the second dorsal segment, and more marked on the left side of the body. By evening of the same day, there was complete anesthesia over the affected areas, and the patient was transferred to the Surgical Service for immediate operation.

Laminectomy was performed on the same evening, by Dr. Elsberg, and a large soft tumor was exposed which lay on the posterior surface of the cord and was so closely connected with the cord that its removal was put off for a second operation. Two weeks

later, the wound was reopened, and the large soft, well encapsulated growth was easily removed. It was 6 cm. in length and at least 1 cm. in width. Pathological report was glioma. Convalescence was uneventful. Within two months most of the motor and sensory symptoms had disappeared, and one month later she was entirely well.

As I have already mentioned, in the large soft tumors which grow around the conus and the roots of the cauda equina, sensation in the lower extremities is either normal or the changes are so slight that the examiner is often in doubt as to the reality of the slight sensory changes. It is most surprising, after the examination has failed to reveal marked sensory disturbances in the lower limbs, to find at operation a large tumor which fills up the lower part of the spinal canal and has grown between and around the nerves of the cauda equina. The absence of sensory disturbances can only be explained on the basis of the soft consistency of the new growth.

Many benign extradural tumors cause for a long time, very vague and indefinite sensory changes. I have operated upon several patients in whom the diagnosis of spinal cord tumor was not made for a long time because of the slight and irregular sensory disturbances. The following patient was watched in the out-patient department of the New York Neurological Institute for many months by Dr. E. L. Zabriskie and by the writer. Distinct objective sensory changes were found long after motor cord symptoms had already been prominent.[2]

Extradural Fibroma of Cord; Laminectomy and Removal. Cure. A. K., aged eighteen years, first came to the out-patient department of the New York Neurological Institute in September, 1913. For three months his friends had told him that he walked with a staggering gait and he himself noticed that he was unsteady on his feet. Several times he was so unsteady that he fell to the ground. This was his only complaint. He was examined by Dr. Zabriskie, but aside from an unsteadiness when he walked, nothing abnormal could be discovered. The patient entered the hospital and repeated careful examinations were made. The reflexes were normal, power in the lower limbs good, no evidence of any sensory disturbance. In October the reflexes in the lower limbs became exaggerated and he developed ankle clonus and Babinski on the left side. At this time there were irregular and very indefinite areas of disturbed sensation on the anterior surfaces of both thighs. After a few weeks stay in the hospital, the patient was discharged and returned to the out-patient department at regular intervals. For a number of months, he was watched by Dr. Zabriskie but no definite areas of disturbed sensation could be made out. In December, 1913, his

[2] I am indebted to Dr. Collins and Dr. Zabriskie for permission to publish this case.

condition grew worse, walking became more difficult so that by the beginning of January, 1915 (seven months from onset of his illness) he was unable to walk or stand unless supported. About this time he began to complain of pain in the right side of the abdomen. He was readmitted to the institute on the service of Dr. Collins on February 11, 1914.

Physical examination now showed the following: The abdominal reflexes were present and equal. The cremasterics could not be obtained. Knee- and ankle-jerks exaggerated, left more than right; exhaustible ankle clonus on left side; Babinski and Chaddock on left. Complete loss of deep muscle sense in left lower extremity. The patient has lost all power in the lower limbs except for slight flexor power at the left knee. The sensory disturbances are very indefinite. There seems to be a slight diminution in tactile and pain sense up to the level of the twelfth dorsal segment. The sensory loss is more distinct over the outer surface of the left leg. It is difficult to say with certainty that there is any disturbance of temperature sense, but it is very slight at the best.

Laminectomy, February 14, 1914 (by Dr. Elsberg): Removal of spinous processes and laminæ or dorsal ninth, tenth, and eleventh. To the right of the tenth dorsal segment, outside of the dura was a bluish tumor mass over which a nerve root was tightly stretched. After division of the nerve root, the growth was easily removed. Convalescence uneventful. All of the symptoms rapidly improved. The patient was presented at the meeting of the New York Surgical Society in April (two months after the operation) subjectively well. One month later, physical examination failed to show any evidence of the previous motor and sensory disturbances. The tumor was reported a fibroma.

Remarks. This case presents a number of features of interest. The presence of motor symptoms long before the appearance of any evidence of sensory disturbance is unusual. When the sensory disturbances finally appeared, they were very indefinite and irregular. Root pain (pain in the right side of the abdomen) appeared only seven months from the beginning of his illness in spite of the fact (as demonstrated at the operation) that the eleventh dorsal root was stretched over the tumor. Finally, the fact of most marked motor disturbance on the opposite side, is of great interest. We have observed this in several instances. It is to be explained by a kind of contrecoup. The spinal cord was pushed to the left by a tumor on its right side, so that the left side of the cord was pressed against the bony wall of the spinal canal resulting in more interference with the left than with the right pyramidal tracts.

Several years ago we had under observation a patient in whom the diagnosis of multiple sclerosis was finally made, in whom sensory disturbances were most marked on the anterior surface of the body.

Since that time, we have examined a number of patients who suffered from a variety of diseases (extradural and intradural tumors, disseminated sclerosis, syringomyelia, stab wound of the cord) in whom the sensory changes on the anterior surface of the body were more marked than on the posterior surface. In several patients, with slight but distinct hypesthesia and hypalgesia on the anterior surface of the trunk and lower limbs, the sensation on the posterior surface was normal. If the diminution of feeling over the front of the body was very marked, that on the back was often much less distinct. I have never, however, seen any difference between the anterior and posterior surfaces of the body when the sensation on the anterior has been entirely lost. While this observation may have been recorded by others, the only reference to the subject I have been able to find is one by Redlich (Neurologisches Centralblatt, 1915, No. 22) who noticed a difference between the sensory disturbances over the front and the back of the trunk in some cases of cerebral hemianesthesia. Recently I operated upon a patient who had a well marked Brown-Sequard syndrome from a stab wound of the back. There was distinct sensory loss affecting all three sensations up to the level of the sixth dorsal segment in front, while, on the back, the loss of sensation was so slight that there was some doubt whether the sensory loss was real or not. At the operation a knife blade two inches long was removed from the spinal canal. It had partially divided the lateral third of the cord.

In a number of patients, also, we have noted that, if pain and thermal sensation was diminished—the disturbance of thermal sense was more marked than that of pain sense. In many cases of spinal compression sensitiveness to pain was markedly diminished over definite areas, while the recognition of and the differentiation between hot and cold was lost entirely.

OBSOLETE MILIARY TUBERCLES OF THE SPLEEN.

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Tuberculosis of the spleen is most commonly observed in cases of widespread miliary tuberculosis. In the not uncommon miliary disease of children and early adolescence, the spleen is usually involved in an intense infection of its tissues. Under these conditions the localization of the infection is mainly through a filtration of the blood by the spleen. The spleen, however, becomes only one of the many tissues in which the microörganisms locate.

The tubercles which arise through the activity of this infection are all of about the same age, showing fairly uniform characters and common stages of development. At autopsy these lesions are seen in the acute or subacute stages, and are scattered in innumerable quantities through the spleen pulp.

The spleen also has been found to be the seat of primary tuberculosis. In the use of the term "primary" it is not meant that the spleen is the portal entry or even the first lesion induced by the invasion of the tubercle bacillus. The term is rather meant to suggest that the pathological process brought about in the spleen is more marked than found elsewhere, and not uncommonly the advanced tuberculous lesion of the spleen leads to a further dissemination into other parts. Thus not a few cases of the so-called primary tuberculosis of spleen show evidence of an older lesion in the thorax with, it may be, very recent tubercles in other tissues. The splenic lesion thus lies intermediate in time and has antedated some of the tuberculous processes of other organs. Not a few of the cases of primary tuberculosis of the spleen have been observed clinically and have received surgical intervention by splenectomy. In these cases it is obvious that although the splenic manifestations have been most prominent during life, no definite information can be offered as to the sequence of events in the tuberculous process. It is interesting that in these cases of primary tuberculosis of the spleen the organ is often found definately enlarged.

To this group of tuberculous infections of the spleen must be added the one here under discussion, the healed or partially healed miliary lesion. Little or no note has been made by students on tuberculosis upon the healing of multiple miliary nodules within the spleen. The early stages of the development of the miliary tubercle is well known and has been much studied. These stages have been accurately followed through the proliferative reactions and the process of caseation. The growth of fibroblasts in the periphery of the advanced nodules has also been discussed, but few have reported observations upon the subsequent fate of the tubercle.

In our earliest observations upon the shot-like, mustard-seed nodules in the spleen we were unconvinced of their tuberculous nature. The fully headed nodule with its concentric layers of fibrous tissue and sharp demarcation from the surrounding spleen pulp, suggested a thrombotic origin of the fibrosis not unlike the formation of phleboliths in the pampiniform plexus of the testis. A further study, however, has given us an opportunity of seeing these nodules in the various stages of fibrosis. The lesions can be followed from the late caseous miliary tubercle with its surrounding fibroblasts to the definite encircling of the area with firm strands of connective tissue. Furthermore in some of the foci with advancing fibrosis evidence of the tuberculous process could be observed on the periphery in immediate contact with the sclerosing ring.

Autopsy No.	Sex.	Age.	Tuberculosis in organs.	Weight of spleen.	Fibrosis in spleen.	Nodules in spleen.	Previous history.
6	M.	42	Obsolete peribronchial glands and spleen	900	Fibrosis	One small calcareous	History of tuberculosis in family. Died of cirrhosis of liver.
16	M.	26	Obsolete spleen and liver	664	Adhesions	Numerous small hard and yellow nodules	No history of tuberculosis. Died of lobar pneumonia.
38	M.	42	Obsolete spleen.	95	Fibrosis.	Many small hard nodules, and one 0.75 cm.	No history of tuberculosis. Died of heart, kidney and arterial diseases.
40	M.	42	Obsolete peribronchial glands and spleen	260	None	Occasional small calcareous nodules	No history of tuberculosis. Died of pyemia.
51	M.	37	Obsolete tracheal glands, spleen and liver	240	Adhesions	Occasional small calcareous nodules and one in accessory spleen	History of tuberculosis not given. Died of chronic empyemia.
98	M.	61	Obsolete peribronchial, mesenteric glands, spleen and liver. Obsolescent of lungs and peribronchial glands	165	Fibrosis	Several small hard yellow nodules	No history of tuberculosis. Died of pernicious anemia.
103	M.	64	Obsolete spleen	160	Fibrosis	One small hard yellow nodule	Died of heart, kidney and arterial diseases.
105	M.	63	Obsolete lung, peribronchial glands, spleen and liver	75	None	Many small hard nodules	No history of tuberculosis. Died of apoplexy (arteriosclerosis.
107	M.	23	Obsolete lung, peribronchial glands, spleen and liver	70	None	Several small hard nodules	Died after severe accident.
122	M.	53	Obsolete peribronchial glands and spleen	140	None	Two small hard nodules	No history of tuberculosis. Died of gonorrheal polyarthritis.
134	M.	43	Obsolete lungs, peribronchial glands & spleen. Obsolescent lungs & retroperitoneal glands	215	None	Many small calcified nodules	Pneumonia two years previously. Died of acute lobar pneumonia.
146	M.	42	Obsolete liver, spleen and mesenteric glands	350	None	Two small calcified nodules	Died of cancer of duodenum.
152	M.	36	Obsolescent lung; obsolete liver and spleen	750	Adhesions	Many hard calcareous nodules	Died following railroad accident.
169	M.	48	Caseous tuberculosis of lungs with cavitation. Obsolete spleen and liver	90	None	One hard shot-like nodule	Died of chronic pulmonary tuberculosis.
173	M.	69	Obsolete lungs, peribronchial glands, liver and spleen	95	None	Occasional small calcareous nodules	Died of fracture of skull.
180	M.	43	Obsolete spleen	150	Adhesions	Two small hard yellow nodules	No history of tuberculosis. Died of acute toxic jaundice.
201	M.	26	Obsolete spleen	?	Adhesions	Many small calcified nodules	Died of diphtheria.
223	M.	20	Obsolete liver and spleen	130	None	Many small seed-like bodies	Died of acute nephritis.
242	M.	21	Obsolete spleen	225	None	Two firm nodules with pin-point areas of necrotic tissue in center	No history of tuberculosis. Died of bronchiectasis and abscess of lung.
298	M.	49	Obsolete spleen	85	None	Single firm yellow nodule	No history of tuberculosis. Died of acute lobar pneumonia.
300	M.	28	Obsolete spleen	190	None	Single hard nodule with necrotic center	No history of tuberculosis. Died of acute lobar pneumonia.
308	F.	39	Obsolete peribronchial glands and spleen	195	None	Many small hard nodules.	No history of tuberculosis. Died of operative hematoma.
315	F.	70	Obsolete lung and spleen	75	Fibrosis	Some small shot-like nodules	History of chronic bronchitis. Died of bronchopneumonia.
333	F.	50	Obsolete spleen	140	Adhesions	Several small calcareous nodules	Died of acute lobar pneumonia.
349	M.	52	Obsolete spleen	200	Fibrosis	One small firm nodule	No history of tuberculosis. Died of syphilitic cirrhosis of liver.

Autopsy No.	Sex.	Age.	Tuberculosis in organs.	Weight of spleen.	Fibrosis in spleen.	Nodules in spleen	Previous history.
350	M.	30	Tuberculous bronchopneumonia. Obsolete and obsolescent peribronchial glands. Acute miliary lungs, spleen and liver. Obsolete spleen	300	None	Many small hard yellow nodules and many gray miliary tubercles	No previous history of tuberculosis. Died of acute miliary tuberculosis. Illness ten days simulating typhoid.
353	M.	25	Obsolete spleen	175	Adhesions	Many firm nodules with calcification	Died of Hodgkin's disease.
359	F.	18	Obsolete peribronchial glands spleen and lung. Obsolescent peri bronchial glands	130	None	Several hard fibroid nodules size of mustard seeds	No history of tuberculosis. Died of acute gastro-enterocolitis.
360	F.	54	Obsolete peribronchial glands and spleen	115	None	One fibrosed nodule	No history of tuberculosis. Died of chronic cholecystitis.
413	M.	36	Caseous tuberculosis of lung with cavitation. Obsolescent peribronchial glands and intestine. Obsolete liver and spleen	225	None	Several hard calcified nodules, the size of mustard seeds	Died of chronic tuberculosis and pyopneumothorax.
422	M.	28	Obsolescent peribronchial glands and lung. Obsolete lung and spleen	90	None	Several small hard nodules, size of mustard seeds	Died of acute lobar pneumonia.
478	F.	36	Obsolescent peribronchial glands Obsolete liver and spleen	195	Adhesions	Numerous round yellow white nodules	Died of rupture of uterus.
480	M.	35	Acute tuberculous peritonitis. Obsolescent peri bronchial, retroperitoneal and omental glands, prostate and lung. Obsolete lung, spleen, liver and adrenal	?	None	Several hard round nodules	Died of tuberculous peritonitis.
516	M.	40	Obsolescent lung. Obsolete spleen and liver	250	None	Several small yellowish nodules	Died of acute lobar pneumonia.
522	M.	63	Obsolete peribronchial and mediastinal glands, and spleen. Acute miliary lung, kidney & spleen. Tuberculous ulcer of larynx	85	None	One small hard calcified nodule	Died of miliary tuberculosis.
534	M.	49	Obsolete spleen	125	None	Many fibrous and calcified nodules size of mustard seeds	Died of acute alcoholism and pneumonia.
541	F.	47	Caseous tuberculosis of lung with cavitation. Obsolete lung, peribronchial and mesenteric glands & spleen	125	None	A single firm white nodule	History of tuberculosis in family. Died of chronic tuberculosis.
567	M.	45	Obsolete spleen	360	None	Few small hard nodules	No history of tuberculosis. Died of appendicitis and peritonitis.
582	F.	42	Obsolescent peribronchial glands and adrenals. Obsolete peri bronchial glands liver and spleen	?	None	Several small hard yellow nodules	Died of Addison's disease.
P–2898	F.	55	Obsolete spleen	175	Fibrosis	Several hard yellow nodules	History of cholelithiasis, jaundice, operation; death from hemorrhage.

To the naked eye the obsolete lesion is characteristic. The shot-like yellow nodules stand in strong contrast to the spleen pulp. The sharp demarcation without an infiltrating fibrosis differentiates the lesion from other sclerosing processes. However, it is impossible by the naked eye to state whether such discrete nodules are fully healed or are only in the obsolescent stage. We have found that nodules, hard and shotty, may still contain within them small remains of caseous material or even evidence on the outer border of a reaction suggesting a still active process. It is, of course, possible that the nodules with peripheral reaction have become the site of a new infection.

The material forming the basis of this report was obtained from 404 autopsies on individuals over ten years of age. In this series of autopsies particular attention was given to noting the presence of tuberculous foci in all parts of the body. Out of the entire series, tuberculosis was noted in 172 cases. The spleen was involved in a tuberculosis process in 69 cases. Of these there were 40 instances in which healed or almost completely healed tuberculous lesions, subsequently to be described, were found.

Of the 40 cases there were 31 males and 9 females. The average age was forty-two, the youngest being eighteen and the oldest seventy. In all but 12 cases old tuberculous lesions were found elsewhere, most frequently in the peribronchial lymph glands or in the lung. In the majority of instances the individual did not suffer from active tuberculosis and clinically no evidence of such infection was observed. Three patients, however, showed a persistent or chronic tuberculosis of the lungs; another died of tuberculous peritonitis, while 2 others died of an acute miliary tuberculosis. Other than these 6 cases the tuberculous lesion or lesions which were present elsewhere than the spleen were in the obsolete or obsolescent stage. In 28 cases an old tuberculous lesion outside of the spleen was found, and in the 6 cases suffering from active tuberculosis this antedated the recent dissemination. An interesting finding was the presence of healed miliary tubercles in the liver. Of these there were 15 cases, in 2 of which the liver and spleen were the only organs involved. These healed tubercles of the liver closely resembled those found in the spleen. They were small, round, and shot-like, without evidences of active tuberculosis in the organ.

Other than the characteristic tuberculous nodules in the spleen, this organ varied very much in its appearance. In weight it ranged from 76 to 900 grams. The average weight was 219 grams while there were twenty-four below 200 grams. As the finding of the old tuberculous lesions in the spleen was in the majority of cases only incident and as the individuals had died of various infections and accidents, the characters found within the spleen cannot entirely be referable to the old tuberculous lesions. It would appear from our

table that the presence of this tuberculous process has no marked influence upon the weight of the organ. The presence of fibrous adhesions about the spleen or of an increase of the fibrous tissue within the spleen, was noted in 15 cases. Such fibrosis or adhesions may have been associated with the acute stage of the tuberculous infection; however, all of these changes cannot be referred to the tuberculous process alone, as cirrhosis of the liver and chronic infections probably played a part in changing the structural character of this tissue. There were many instances in which no characteristic change was to be noted in the splenic structure other than the isolated fibrous nodules of old tuberculosis. In 2 cases the old and discrete tuberculous processes of the spleen were associated with more recent miliary tubercles in the active and progressive stages. This would indicate a second dissemination of tubercle bacilli reaching the spleen.

The miliary tubercle of the spleen in the healed or almost healed state differs quite markedly in its appearance from similar lesions in other organs save the liver. It appeared in the character of a small nodule of hard consistence and usually spherical. The type most commonly met with appeared like a small yellow concretion about the size, shape, and color of a mustard seed. Occasionally larger nodules were found, of somewhat irregular shape and measuring up to about 0.75 cm. in diameter. These nodules were irregularly scattered through the spleen substance, and their yellow color was in sharp contrast to the dark red pulp of the organ. They were found directly beneath the capsule or sprinkled through the parenchyma of the spleen. Their outer border was sharply demarcated from the spleen tissue, and they are quite easily removed from the surrounding structure. In their periphery there was no evidence of fibrosis extending into the surrounding parts. At times in shelling out the nodules the outer capsule was found to remain in the spleen tissue forming a small cup-like cavity. The discrete character of the nodules and the absence of change in their immediate vicinity was always striking.

The number of these nodules varied from a few to a large number. Occasionally small clusters were found, but in the majority of instances the discrete masses were irregularly scattered at some distance from each other. The macroscopic appearance of the tissues forming the nodules have been fairly uniform. They were hard and shot-like, and the outer coats consisted of concentric layers of fibrous tissue which could be removed in successive laminæ. The centers of the nodules were either hard and calcareous or fibrosed, some of them still showing soft necrotic material. The necrotic substance when present formed very small, almost pin-point areas in the immediate center. In a few instances a relationship between the nodules and the vascular channels was observed.

The finding of 12 cases in which tuberculous foci were alone

found in the spleen is remarkable. At first sight one would be tempted to suggest that the finding was dependent upon a careless search for other lesions. In a number of cases, however, a distinct note was made at the time of autopsy that this was the only focus discovered. In these cases the splenic lesions differed in no way from those found in the remaining series.

There is one common characteristic possessed by all of the nodules which we have examined. This consists of the mature concentric layers of connective tissue which surround them and sharply demarcate the nodule from the spleen pulp. The spleen tissue immediately

FIG. 1.—Spleen with obsolete miliary nodules of tuberculosis.

beyond the outer border of the nodule commonly showed no evidence of reaction, nor was its architecture changed. The fibrous tissue in the nodule did not send any trabeculæ into the surrounding tissue. This sharp line of demarcation in the absence of any response in the spleen pulp was quite remarkable. In some of the more recent lesions, those that had not advanced to complete healing showed more or less lymphocytic infiltration in the tissues immediately surrounding the nodules, and in 4 instances this was accompanied by the presence of small and recent tubercles in the progressive and active stages. In some cases it appeared that these

tubercles were associated with and dependent for their existence upon the main tubercles which had not reached the final stage of healing. In 2 instances recent tubercles were found in the spleen

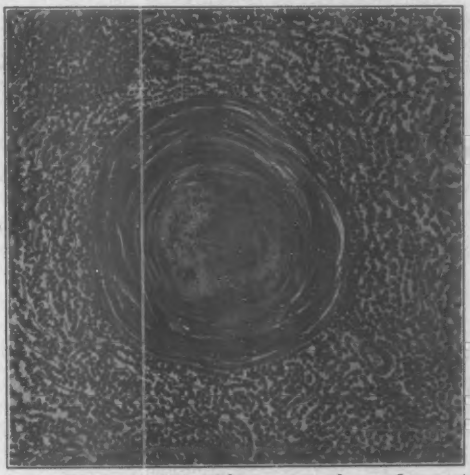

FIG. 2.—Fibrosed nodule with remnants of central necrosis.

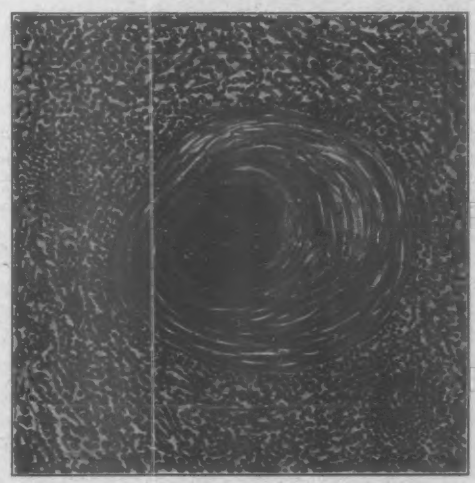

FIG. 3.—Fibrosed nodule with central calcification.

quite unassociated with the old nodules, but indicating a new hematogenous miliary distribution, as was indicated in the generalized miliary tuberculosis found elsewhere.

The size of the obsolete tuberculous lesions of the spleen indicated that during the active stage they consisted not of a single tubercle but of several closely approximated lesions. It is probable that, like the development of the ordinary miliary tubercle, the process began in a single tubercle, but with the development of necrosis and the multiplication of the tubercle bacilli a number of new tubercles were developed in the periphery. Thus numerous tubercles developed upon the circumference of the enlarging area until a size was attained which was readily distinguished by the naked eye.

The disposition of these old foci in the spleen was irregular and at times difficult to define. In some of them the remains of the central artery of the Malpighian body could still be seen within the fibrosed tubercle. These arteries were still patent and the fibrous tissue immediately bounding them was disposed in a direction concentric with the vessel. At other times it appeared as if the tubercle had developed within the pulp substance at a distance from the Malpighian body and unassociated with the trabeculæ of the spleen.

Although the nodules have, on naked-eye examination, a very similar appearance, and though they all have the common characteristic of being surrounded by a dense laminated connective tissue the central area may differ quite widely. In some the concentric layers of connective tissue continued throughout the nodule; others contained a small mass of granular necrotic material; the remains of former caseation in the center. The latter showed no evidence of an active process insofar as a tissue reaction was concerned. The necrotic material was firmly bounded by a wide border of dense connective tissue without evidence of lymphocytes, endothelial cells, or giant cells. A varying amount of calcification was also seen in these areas of necrosis. At times this consisted of a fine granular precipitate while in others a definite concretion formed a central nucleus.

The manner of laying down of the connective tissue is interesting. In the early development of the miliary tubercle in the spleen the proliferative response giving rise to the new cells of the tubercle leads to the crowding aside of the essential tissues of the area. The fine reticular stroma with its lymphocytes and endothelial cells is pushed outward, so that in the immediate periphery of the tubercle they appear to lie in a concentric fashion. At this early stage there is no increase in this reticular tissue. Soon, however, this neighboring stroma without actual proliferation increases the thickness of its strands by the accumulation of hyalin or collagen. It has thus been not uncommon to find a peripheral border of a heavy collagen containing connective tissue forming a lacework surrounding the tubercle, from which the lymphocytes gradually disappeared. When the lymphocytes accumulate it is usually to the outer side of this stroma. This connective-tissue boundary continues to exist with the increasing growth of the tubercle, but not until a reparative

process appears about the active foci does the original connective-tissue capsule increase to any definite degree. The laying down of new connective-tissue bands takes place on the inner side of this connective-tissue layer. Fibroblasts make their appearance in the small tubercles bounding the caseous center and gradually the characteristic architecture of the tubercle becomes disturbed until the giant cell lying within the jumble of fibroblasts and a few endothelial cells is all that remains of the active granuloma As the fibroblasts gradually lay down the permanent collagen fibers they are disposed in a concentric fashion. The disappearance of the fibroblast itself is rapid until nothing remains save the dense laminated collagen fibers. It was very apparent in these nodules that after the disappearance of the active process the new growth of connective tissue advanced but slowly. The caseous material in the center gave no evidence of tissue stimulation, and its absorption and removal was a slow procedure. Thus advancing fibrosis toward the center was a matter of time during which the central débris was being slowly removed.

Many sections of the fibroid masses, as well as of nodules with small caseous centers, were searched for tubercle bacilli but none were found. I would place no individual stress upon the negative finding obtained in material which had been stored in preservatives for more than a year, but as we have had similar results in dealing with tissues of more recent origin, I am inclined to view these strucures as devoid of infection. At what stage in the healing process the microörganismas are destroyed cannot be stated, but it is probable that the event bears comparison with similar lesions in the lymph glands, as has been described by Warthin.

In 2 cases of recurrent infection of the spleen we have demonstrated tubercle bacilli in the progressive tissue lesions lying outside of the hard nodules, while no bacteria were found in the healed lesion. As we have previously stated these peripheral tubercles may have been a hematogenous reinfection of the spleen, or it may be that the bacteria had escaped from the primary miliary foci during the earlier stages of their development. In the latter case, if true, the infection remained latent over a considerable period, so that the difference in the tissue reaction between the primary and secondary lesion was very apparent.

Discussion. The evidence that we have here presented of healed or healing miliary tuberculosis of the spleen has an interest both from the clinical and pathological view-point.

In the majority of the cases the distribution of the tubercle bacillus to the spleen had taken place from small foci having no clinical significance. The findings indicate that the peribronchial glands were most frequently the areas from which microörganisms were disseminated by way of the blood stream. It is probable that, at the time of the bacillary distribution, several organs became

the point of localization, and we have evidence that in 15 cases the liver was simultaneously involved with the spleen. In the majority of instances, however, miliary lesions of contemporary infection were lacking elsewhere. It is obvious that scattered miliary lesions induced in many tissues escape our eye after the process of healing is complete and when the local damage is of small extent. We cannot claim that in our series of autopsies all cases of healed miliary lesions of the spleen were observed, as isolated nodules may readily escape detection. It is, however, striking that as many as 40 cases should have come to our notice in a series of 404 autopsies on individuals over ten.

The absence of clinical data of any symptoms, whereby the time of infection of the splenic tissues can be indicated, gives us no opportunity of determining the age and rapidity of the healing process of localized miliary tuberculosis of the spleen. The early fibrosis developing about tuberculous areas after a period of six weeks or several months has been well studied in man and animals. Such reactionary fibroses, however, are still in the proliferative stage when fibroblasts and young connective-tissue cells are laying down an outer wall about the area of necrosis. The majority of lesions in our cases, however, were much more advanced and were devoid of evidence of active proliferation except in the instances where more recent recurrent infection had localized in the vicinity of the old lesion. The concentric bands of connective tissue were in the mature state, and in some instances in a process of hyaline transformation. Months of time would bring little alteration in their structure. It is well seen that such encapsulation would permit only of slow organization of remnants of the caseous process. In some instances calcification of the central area supervened but in others a fine and granular necrotic material still remained. Whether any infection was still present in the central areas of necrosis could not be finally determined. We were unable to demonstrate tubercle bacilli in this material, but whether latent infection was still available must remain unanswered until inoculation experiments are undertaken. As the material with which we were dealing had been preserved from autopsies performed at different times in the past five years, we were unable to carry out all of the studies necessary to clear up many of these points.

A point worthy of comment is that the presence of these old tuberculous foci had no marked effect upon the uninvolved portion of the spleen. In a number of cases adhesions were found; in a few others there was fibrosis. By no means, however, was the fibrosis marked and often when noted it was more relative than real. Furthermore, in some cases the fibrosis had a direct relation to an intercurrent disease process. Likewise there was no constant evidence of splenic enlargement resulting from the presence of old tuberculosis. It has been indicated that in the so-called primary

tuberculosis of the spleen one of the not unusual manifestations is the increase in weight and volume of the organ. The reported cases of primary tuberculosis of the spleen were observed in the acute or obsolescent stage. In these instances the focus of infection was of fair size, often occupying a considerable portion of the organ. Under these conditions the spleen showed definite enlargement. It is not uncommon that in acute miliary tuberculosis in which the spleen among other organs becomes the site of innumerable tubercles, its weight is materially increased. It may well be that during the acute process of infection of the cases reported in our series, the spleen was more or less enlarged. The condition, however, was transient leaving no characteristic organic change in its internal structure.

The distribution of the tuberculous infection was hematogenous. Whether the primary portal of entry was through the respiratory or alimentary system is immaterial. Undoubtedly, however, the infection primarily found localization in some other tissues where, after multiplication of the microörganisms and destructive changes in the involved structure, the bacteria found entrance into the blood stream. That no fatal outcome resulted at the time of this blood-stream dissemination indicated that relatively few bacteria were discharged from the initial focus. We have interesting evidence, therefore, that the quantity of infection of miliary tuberculosis varies greatly, and that the outcome of such distribution depends upon the relation between the amount of infection and the resistance of the tissues in which the bacteria locate. In these cases of old tuberculous foci in the spleen we have observed encapsulated nodules varying in number from one to very many.

A considerable interest has recently been taken in the role of the lymphocyte in tuberculosis. Bartel believed that he was able to demonstrate, by experiment, that a direct antagonism existed between lymphatic tissues and the tubercle bacillus. Primarily, it was found that a hyperplasia of the lymphoid structures along with an endothelial proliferation took place. These lymphatic tissues not only act as filters for the microörganism, but also offer a protective mechanism for the body. In many instances the infection of animal tissues by the tubercle bacillus is unassociated with structural change, even though the microörganisms are present in the tissues. Bartel has been able to demonstrate the tubercle bacillus within lymph glands in which no other change than hyperplasia had occurred. These bacteria he found were much reduced in virulence. Lewis and Margot found that there was a relation between the function of the spleen and the resistance of an animal to tuberculosis. Commonly after the inoculation with tubercle bacilli the spleen became enlarged. In mice it was found that splenectomy prolonged the life of the inoculated animals. No explanation could be offered for these apparently divergent results.

Ths importance of the spleen in counteracting infection, not only within its own tissue but also of a systemic kind, was shown in the experiments of Hektoen and of Simonds and Jones. These authors brought about partial destruction of the spleen by the application of the roentgen ray. After intense or prolonged exposure the animals developed a greater susceptibility for infection. This susceptibility appeared to be the result of a decrease in the lysins of the blood as well as a decided inhibition in the production and activity of the leukocytes. However, as the use of the roentgen-ray on small animals is not limited in its influence upon the spleen alone, it is possible that the change in the quantity of immune bodies is also dependent upon the effect of the rays upon the other hemopoietic organs. Somewhat more confusing results have been obtained by the use of benzol. This substance has a marked influence in depressing the production of leukocytes by the bone marrow, at the same time it was shown by White that prolonged treatment of rabbits by benzol led to the development of a much enlarged spleen. This occurred even when the leukocytes of the blood had been reduced more than one-half. Under these conditions of an enlarged spleen and diminished leukocytes the animal showed an increased susceptibility to the tubercle bacillus as compared to the untreated animals.

There appears, therefore, to be good evidence that the spleen has a definite relation to the development of immune bodies in various animals. This function is probably a limited one, and is similar to that possessed by other hemopoietic tissues. Whether the resistance of the spleen to infection differs greatly with the various microörganisms is not clear, but it would seem that, like other lymphatic tissues, its antagonism to the tubercle bacillus is quite marked.

Of the 40 cases of healed miliary tubercles of the spleen, 15 showed similar lesions in the liver. The liver nodules were identical with those in the spleen, being round and hard and of the size of mustard seeds. They were distributed irregularly through the liver substance, and usually were few in number. More frequently they were found in the periphery of the lobule, in direct contact with the fibrous tissue of the portal systems. Their sharp demarcation from the surrounding liver tissue was as striking as in the spleen, and the absence of associated tissue change in other parts of the liver was constant. Whether the microörganisms located in the liver at the time of the general hematogenous distribution, or whether the liver infection was gained by the portal blood from the spleen cannot be stated. Both routes of infection are available, and a portal distribution during the active process in the spleen might readily occur.

In view of the high incidence of liver infection in all cases of tuberculosis, as is claimed by some, it is remarkable that healed miliary

nodules do not appear more frequently. If, as Ullom states, tuberculosis of the liver develops in from 70 to 100 per cent. of the cases, the mode of distribution must in large part be hematogenous, and Rolleston believed mainly by the portal vein. In our own observations we have failed to find tuberculosis of the liver as frequently as stated, though we have never undertaken a systematic search by the microscope. As is observed by all, the tuberculous lesions of the liver are most often of insignificant size and discovered only by microscopic search. The lesions which we have observed associated with the spleen nodules were all recognized by the naked eye at the autopsy table. Their character was so uniformly similar to those in the spleen as to suggest a synchronous deposition. Moreover, they would also indicate a tissue resistance to this infection equal to that of the spleen, suggesting a systemic as well as a local organic origin for the immunity. In no instance where healed miliary tubercles were found in the spleen had the liver infection progressed to conglomerate tubercles or cavitation. Even in those cases of pulmonary tuberculosis in which the tissue progressed to caseation and cavitation of the lungs the foci in the liver and spleen remained small and were well advanced in healing. These differences in the healing process of various tissues offer interesting studies in tissue immunity.

We find but little reference in the literature to the presence of healed miliary lesions in the spleen. Abbott in the *Catalogue of the McGill Medical Museum* mentions one specimen presented by Adami of the character as we have described. In an analysis of 1000 autopsies Adami and McCrae found evidence of healed tuberculosis in 151 cases and of these, healed lesions were present in the spleen twice while obsolescent lesions were seen four times. Winternitz has given a very full review of the work on tuberculosis of the spleen, in which he makes particular reference to the so-called primary tuberculosis, a condition quite different from that which we have under discussion. The lesions described by him usually refer to large caseous masses which have led to much enlargement of the spleen to be recognized clinically. A considerable number of these cases were treated surgically by splenectomy. Although the spleen is spoken of as the seat of acute or subacute miliary infection no reference is made to the healed lesion. The frequency of splenic involvement in tuberculosis is given by Reinhold, who found tuberculosis of the spleen in 67 per cent. out of 428 cases of tuberculosis in children, and in 19 per cent. out of 836 cases in adults. In our own series of 404 autopsies tuberculosis was present 172 times and the spleen was involved in 69 cases. In 40 of the latter healed miliary lesions were found in the spleen, 2 of them showing a reinfection with a fresh crop of tubercles. Sternberg in a discussion upon peculiar types of tuberculosis with characters of pseudoleukemia noted the tendency to fibrous encapsulation of tuberculous processes in the spleen. Colet and Gallavardin referred

to the finding of partly sclerosed nodules in the spleen of a man, aged sixty years. The liver in this case also had nodules which were still caseous. The report on focal tubercuolsis of the spleen by Fischer deals with subacute lesions in which caseation occupies the center of the nodule while the periphery is made up of proliferating epithelioid and giant cells. None of the lesions observed by him had reached the obsolete stage. Brohl excised the spleen of a patient aged forty-eight years, and found six small yellow concretions which contained calcium carbonate and phosphate, and which he believed had their origin in phleboliths.

More comparable to the described lesions of the spleen are those reported by Warthin occurring in the mesenteric glands. Warthin claimed to find evidence of healed tuberculosis in the mesenteric glands with great frequency. The tissue changes consisted in part of hyaline deposits as well as small fibrosed nodules with central débris and a peripheral laminated structure. The latter lesions appeared very similar to those which we have observed in the spleen. On no occasion, however, have we found the centers to consist of a hyaline substanec. The hyaline transformation of the neighboring stroma was frequently observed in the spleen in the presence of tuberculous foci. Warthin found similar hyaline and sclerosed masses in the bronchial glands of adults.

A word must be said about the 12 cases of healed miliary tuberculosis of the spleen in which no other focus was found in the body. As we have previously indicated, search was made at the time of autopsy for other tuberculous manifestations, and none were found. We cannot but doubt that some unrecognized focus had existed near the point of entrance of the infection, but that recognizable tissue change was no longer evident. The splenic infection had undoubtedly developed through blood infection in which other organs had also received localized foci. It would appear that the tuberculous process had been dealt with unequally in the various tissues, all save the spleen clearing themselves of the invading organism before permanent damage was done. In the spleen, temporary tissue destruction was brought about with subsequent complete healing. In these cases it would appear that the resistance of the spleen to tuberculous involvement was not so great as in other tissues. These findings would indicate that a tuberculous bacteriemia may occur in the absence of an advanced localized focus of infection and that a miliary distribution may be overcome by the individual tissue resistance.

Conclusions. In a series of 404 autopsies, tuberculosis was met with in 172 cases. The spleen was involved 69 times, and in 40 of these miliary lesions were completely or almost completely healed by fibrosis.

The average age was forty-two years and the youngest was eighteen years. Six of the cases showed a persistent tuberculosis in other organs. In 15 cases the liver also contained healed miliary tubercles.

In none of the cases had there been recognizable clinical manifestations of splenic involvement. The spleen was not enlarged. In 12 cases with healed miliary tubercles of the spleen no other tuberculous process was found.

The splenic infection was a hematogenous one arising most commonly from antecedent foci in the lungs or peribronchial glands. Those cases in which no primary tuberculous focus was found probably had a similar mode of origin in which, however, the initial focus was of minor extent unrecognizable at the time of autopsy. We would point out that the fibroses which are observed in anthracotic peribronchial glands are difficult of analysis as indicating a preceding infectious origin of the fibrosis.

The healed splenic tubercles are recognized only by careful search and complete gross sectioning of the tissues of the organ. The presence of the healed miliary tubercles of the spleen indicates the frequency of a tuberculous bacteriemia from which the tissues may entirely recover. The different organs demonstrate a variable resistance to the tuberculous infection. Reinfection may take place in the spleen.

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THE ASSOCIATION OF GASTRIC SYMPTOMS IN NEPHRITIS WITH RETENTION OF NITROGENOUS WASTE PRODUCTS IN THE BLOOD.[1]

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Since the time of Richard Bright it has been recognized that renal disorders are accompanied by digestive disturbances. The

[1] Read before the American Gastro-enterological Association, Washington, D. C.

pathological basis for this association has been the source of much speculation for the reason that there are no physiological facts which adequately explain it. The symptoms occur in all stages of the disease, from the most incipient to the furthest advanced. Many cases of unrecognized nephritis have only symptoms of dyspepsia. We have been particularly impressed with the number of cases of latent nephritis sent to the hospital with a diagnosis of gastric ulcer or of toxic vomiting. The more common symptoms from which patients of this type complain are nausea, vomiting, loss of appetite, flatulency, abdominal distress, usually without definite relationship to meals, and headaches, frequently of the migrainous type. Owing to the depressed gastric secretion the diagnosis of asthenic gastritis is occasionally made. On account of the toxic character of the vomiting these patients are frequently told that they are suffering from enterogenous intoxication.

In view of the important advances recently made in the estimation of the various nitrogenous waste products which accumulate in the blood (and tissues) in nephritis it appeared of interest to compare the type and extent of this retention with any gastric symptoms which might occur. The end-products of nitrogenous metabolism which deserve consideration are the uric acid, urea, and creatinin. As has already been pointed out in contributions from this institution,[2] uric acid is normally the most difficult and creatinin the easiest to eliminate. It is not surprising, then, that very early cases of nephritis should show a retention of uric acid without any corresponding retention of urea or creatinin, while cases in the last stages of the disease should be the only ones in which a decided increase in creatinin is encountered. Following this scheme we have divided the cases we propose to discuss into two groups, viz., those showing high creatinins and others in which the high uric acid was the prominent feature. This arrangement has been made for the reason that the retention of creatinin has been found to be of great prognostic value in nephritis[3] while the uric acid appears to be an early diagnostic sign. The cases showing marked nitrogen retention, particularly with respect to the creatinin, will first be considered. The similarity in the gastric symptoms in this group of 10 fatal cases (see Table I) is very striking. It is worthy of note that 3 of these cases (II—T. D., VI—E. P., and VII —J. W.) were called to my attention on account of their gastric symptoms. Although examination at once revealed the fact that these patients were suffering from nephritis, the gravity of the situation was not appreciated until a blood examination disclosed a marked retention of creatinin. These cases greatly impressed me and, in a measure, suggested the title of the present paper. Their histories are worthy of brief review:

[2] Myers, Fine, and Lough: Arch. Int. Med., 1916, xvii, 570.
[3] Myers and Lough: Arch. Int. Med., 1915, xxi, 536.

CASE II.—T. D., male, aged thirty-four years, at the time of admission to the hospital, on January 13, 1915, was able to be up and about. His chief complaint was vomiting and pain in the epigastrium of five to six months' duration. A chemical blood examination was made and gave a creatinin of 7.8 mg. to 100 c.c., showing that the patient was in the terminal stages of interstitial nephritis. He died on March 23, 1915.

CASE VI.—E. P., female, aged forty years, was admitted to the hospital with a history of persistent vomiting for the previous two months. Physical examination showed a fairly well-nourished woman with no evidence of edema. The chemical examination of the blood not only established the diagnosis of nephritis, but the high creatinin (8 mg. to 100 c.c. of blood) gave a fatal prognosis. The woman died six weeks after leaving the hospital.

CASE VII.—J. W., male, aged thirty-four years, walked to the hospital and was admitted on February 22, 1915, complaining of headaches, nausea, vomiting, and constipation. A blood examination gave a creatinin of 8.3 mg. Clinically the patient quickly improved and was continuously up and about the ward. He repeatedly requested to be allowed to go home, but as the creatinin of the blood remained high, he was persuaded to remain. He was up on April 14, but on becoming faint was put to bed, gradually declined, and died on April 16, 1915.

Figures for the CO_2-combining power of the blood (according to Van Slyke's method) are given for 5 of the 10 cases. Although these are all low it is scarcely believed that the acidosis bore a causal relation to the vomiting. Although we have no definite evidence showing that the nitrogenous waste products have such a relationship it is of some significance that the gastric symptoms seem to vary, to a certain extent, with the amount of retention.

In Table II are tabulated 12 cases with gastric disturbances in which the special feature of the blood analysis is the high uric acid. Many of these cases showed symptoms directly comparable with the preceding group, although none of them was terminal. In general the symptoms were more mild than the preceding, but it seems safe to conclude that they were the early manifestations of the same general condition.

In cases of migraine the estimation of the uric acid of the blood has been of great value in detecting a latent nephritis. Four years ago we were impressed with a case of this character.

D. L., aged forty-five years, had suffered from periodic attacks of typical migraine for the previous five years. These attacks were intense and had resisted all forms of treatment both here and abroad. Examination of his blood proved to be normal with the exception of a uric acid retention of 5 mg. per 100 c.c. When treatment was instituted to reduce the uric acid accumulation in the blood the sick headaches suddenly stopped and have not returned. The only

TABLE I.—GASTRIC SYMPTOMS AND BLOOD FINDINGS IN FATAL CASES OF NEPHRITIS.

Case.	Age.	Sex.	Urine.		Blood-pressure.		Phthalein 2 hrs. Per cent.	CO_2 combining power. C.c. to 100	Blood-sugar. Per cent.	Uric acid.	Urea nitrogen.	Creatinine.	Gastric symptoms.	Result.
			Albumin.	Casts.	Systolic.	Diastolic.				Mg. to 100 c.c. of blood.				
I—S. H.	37	M	++	++	220	138	0	..	0.14	14.3	262	22.2	Vomiting; gaseous eructations	Died.
II—T. D.	34	M	+++	+	210	105	0	..	0.14	14.3	152	20.5	Nausea; vomiting; epigastric pain	Died.
III—I. D.	17	F	++	++	182	138	0	..	0.19	27.0	209	20.0	Vomiting; abdominal pain	Died.
IV—P. J.	43	M	+++	−	..	..	0	31	0.25	12.5	162	20.0	Vomiting 2 mos.; duration	Died.
V—E. C.	50	F	++	−	210	100	..	..	0.09	22.4	236	16.7	Vomiting 2 yrs.; constipation; poor appetite	Died.
VI—E. P.	40	F	+++	+	205	145	0	39	0.19	4.2	46	12.5	Vomiting 4 mos.; epigastric pain; constipation	Died.
VII—J. W.	34	M	++	++	220	100	trace	..	0.14	8.7	144	11.0	Nausea and vomiting; constipation	Died.
VIII—O. G.	22	M	++	−	225	115	23	45	0.13	7.3	65	4.5	Vomiting 2 weeks	Died.
IX—P. L.	47	F	+	−	127	85	13	27	0.16	13.3	28	4.3	Vomiting; no relation to food intake; constipation	Died.
X—M. S.	62	M	++	+++	195	100	18	20	0.08	7.3	30	4.0	Vomiting.	Died.

Normal blood findings: CO_2 combining power 54 c.c. per 100, sugar 0.10 per cent., and uric acid 2 3, urea N 12-15, and creatinine 1–2.5 mg. to 100 c.c.

TABLE II.—GASTRIC SYMPTOMS AND BLOOD FINDINGS IN NON-FATAL CASES OF NEPHRITIS.

Case.	Age.	Sex.	Urine.		Blood-pressure.		Phthalein 2 hrs. Per cent.	Blood-sugar. Per cent.	Uric acid.	Urea nitrogen.	Creatinine.	Gastric symptoms.	Result.
			Albumin.	Casts.	Systolic.	Diastolic.			Mg. to 100 c.c. of blood.				
I—M. S.	41	F	+	++	140	75	53	0.09	6.7	22	1.5	Vomiting; abdominal pain; diarrhea	Improved.
II—A. R.	57	M	−	−	130	70	40	0.12	6.3	22	2.5	Gaseous eructations; no vomiting; constipation	Unimproved.
III—J. C.	69	M	+++	−	150	100	20	0.11	6.3	40	1.5	Vomiting; diarrhea	Unimproved.
IV—P. P.	28	M	+	+	135	70	61	0.11	6.3	15	2.4	Vomiting; regurgitation of food; appetite poor	Improved.
V—M. S.	46	F	+	+	210	150	51	0.12	6.1	12	2.6	Vomiting; flatulency; constipation	Unimproved.
VI—L. B.	50	M	−	−	160	95	40	0.11	5.4	11	0.9	Vomiting; no relation to food intake	Improved.
VII—N. B.	71	M	+	+	130	75	54	0.11	5.4	17	2.8	Occasional vomiting	Improved.
VIII—A. B.	38	F	−	+	110	80	50	..	5.0	27	3.3	Vomiting; gaseous eructations	Improved.
IX—G. G.	61	M	+	+	210	110	48	0.11	4.8	22	3.4	Nausea and vomiting; constipation	Improved.
X—L. K.	72	M	+++	++	200	100	..	0.12	4.6	37	1.8	Epigastric pain	Improved.
XI—F. S.	67	M	+	+	125	90	16	..	4.2	10	1.5	Occasional vomiting	Improved.
XII—S. F.	58	F	+	+	190	70	44	0.12	3.7	22	3.2	Nausea and vomiting; epigastric pain	Improved.

other evidence of nephritis during the past four years has been an occasional faint trace of albumin in the urine with a systolic blood-pressure of 155 and a diastolic of 95. These conditions have been transitory.

Aside from the stomatitis and ulcerative colitis of uremia the gastro-enteric symptoms of nephritis are probably central. Evidence is lacking that uric acid, urea, and creatinin are toxic in themselves. The amount of their retention is a probable index, however, of the accumulation of unknown substances which may possess some toxic importance. A poor oxidation of creatinin in the absence of its excretion would give methyl guanidin, a substance of known toxic properties. The possible relation of such substances to the gastric symptoms of nephritis is, at present, only problematical.

NOTES ON CASES IN TABLE I.

CASE I.—S. H., male, aged thirty-seven years. Headaches; dizziness; constipation; alcoholic; had stomach trouble five months; vomiting; edema of feet and ankles. Diagnosis: chronic interstitial nephritis; died.

CASE II.—T. D., male, aged thirty-four years. Vomiting; epigastric pain for five to six months; alcoholic; constipation; had scarlet fever; weight in abdomen after food intake. Diagnosis: chronic interstitial nephritis; died.

CASE III.—I. D., female, aged seventeen years. Frontal headaches; epigastric pain; dizziness; vomiting; dyspnea; tachycardia. Diagnosis: chronic interstitial nephritis; died.

CASE IV.—P. J., male, aged forty-three years. Gastritis; diarrhea; headaches; dizziness; vomiting two months; edema of feet and ankles. Diagnosis: chronic interstitial nephritis; died.

CASE V.—E. C., female, aged fifty years. Dizziness; inability to pass urine; vomiting for past two years; no relation to food intake; constipation; nycturia. Diagnosis: chronic interstitial nephritis; died.

CASE VI.—E. P., female, aged forty years. Vomiting four months with headaches; slight epigastric pain; vomiting; bears no relation to food intake; constipation. Diagnosis: chronic interstitial nephritis; died.

CASE VII.—J. P., male, aged thirty-four years. Syphilis sixteen years ago; marked alcoholic; dyspnea; headaches; vomiting; edema of face and lower extremities fifteen months. Diagnosis: chronic interstitial nephritis; died.

CASE VIII.—O. G., male, aged twenty-two years. Fainting spells; impairment of vision; vomiting two weeks; alcoholic. Diagnosis: chronic interstitial nephritis; died.

CASE IX.—P. L., female, aged forty-seven years. Cough for three years; headaches; dizziness; palpitation of heart; constipa-

tion; vomiting; no relation to food intake; arthritis of right elbow. Diagnosis: carcinoma of liver; died.

CASE X.—M. S., male, aged sixty-two years. Headaches; occasional vomiting spells; dyspnea; increased frequency of urination; edema of feet and ankles; arthritis for ten years (?); enlargement of heart to right. Diagnosis: chronic interstitial nephritis, endocarditis; died.

NOTES ON CASES IN TABLE II.

CASE I.—M. S., female, aged forty-one years. Scarlet fever; diphtheria as child; abdominal pain; frequency of urination; diarrhea; vomiting; dyspnea. Diagnosis: neurasthenia; improved.

CASE II.—A. R., male, aged fifty-seven years. Constipation; gaseous eructations; nycturia; painful urination; no vomiting. Diagnosis: carcinoma of stomach and liver; unimproved.

CASE III.—J. C., male, aged sixty-nine years. Vomiting; diarrhea; edema of feet and ankles. Diagnosis: chronic interstitial nephritis; endocarditis; transferred; unimproved.

CASE IV.—P. P., male, aged twenty-eight years. Regurgitation of food; moderate alcoholic; occasional vomiting spell. Diagnosis: gastric ulcer (?); improved.

CASE V.—M. S., female, aged forty-six years. Weakness; anemia; headache; vertigo; cardiac pain; diarrhea; flatulence; epigastric pain; vomiting. Diagnosis: chronic interstitial nephritis; unimproved.

CASE IV.—P. P., male, aged twenty-eight years. Regurgitation of food; moderate alcoholic; occasional vomiting spell. Diagnosis: gastric ulcer (?); improved.

CASE V.—M. S., female, aged forty-six years. Weakness; anemia; headache; vertigo; cardiac pain; diarrhea; flatulence; epigastric pain; vomiting. Diagnosis: chronic interstitial nephritis; unimproved.

CASE VI.—L. B., male, aged fifty years. Headache; pneumonia eight years ago; vomiting spells every ten to fourteen days; no relation to food intake. Diagnosis: chronic interstitial nephritis; cecal stasis; improved.

CASE VII.—N. B., male, aged seventy-one years. Scarlet fever; constipation; pain in chest; difficulty in voiding. Diagnosis: chronic interstitial nephritis; improved.

CASE VIII.—A. B., female, aged thirty-eight years. Headache; stomach trouble seven months' duration; gaseous eructations; dyspnea; vomiting; accentuated P^2. Diagnosis: mucous colitis; improved.

CASE IX.—G. G., male, aged sixty-one years. Constipation; dizziness; vomiting three years; dyspnea; accentuated A^2. Diagnosis: chronic interstitial nephritis; hemiplegia; improved.

CASE X.—L. K., male, aged seventy-two years. Pneumonia; diphtheria; epigastric pain; relieved after food intake. Accentuated A^2. Diagnosis: chronic pancreatitis; improved.

CASE XI.—F. S., male, aged sixty-one years. Dyspnea; occasional vomiting spell; regardless of food intake; headache; weakness. Diagnosis: chronic interstitial nephritis; improved.

CASE XII.—S. F., female, aged fifty-eight years. Arthritis in all joints (?); headache; dizziness; constipation; pains in shoulder; epigastric pain; nausea and vomiting; jaundice. Diagnosis: chronic interstitial nephritis; improved.

CONCLUSIONS. Gastric symptoms are among the most common early symptoms of nephritis. In cases with obscure gastric disturbances the chemical examination of the blood has been found very valuable. Several cases are reported in which the estimation of the blood creatinin not only showed that the patients were suffering from severe nephritis, but gave a fatal prognosis. In some of the earlier cases the blood uric acid was of value as an early diagnostic sign.

STUDIES IN THE PHYSIOLOGY AND PATHOLOGY OF THE STOMACH AFTER GASTRO-ENTEROSTOMY.[1]

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THE operative treatment of ulcer of the stomach or duodenum is in the largest percentage of cases a curative one. Experiences, however, have demonstrated that the continuous repetition of instances demonstrating the splendid results obtained by operative interference is constantly and not infrequently being disturbed by a group of cases in which some of the preoperative symptoms persist after the surgical interference or in which new symptoms of an apparently different nature supervene during or after the period of recovery.

[1] Read by invitation at the Nineteenth Annual Meeting of the American Gastro-enterological Association, held at Washington, D. C.

Our efforts have been bent to studying the physiology and pathology of the stomach after operative procedures, and we have attempted by a careful analysis of the data, which we have thus far collected, to define and separate these cases into groups. We base the classification upon the clinical symptoms, the chemical findings, and upon a study of the gastric motor mechanism in the hunger state by means of kymographic tracings. For this last we have made use of the physiological methods employed by Cannon and Carlson, and have controlled the observations by radiographic examinations made by Dr. L. Jaches and his associates in the department of roentgenology.

This study comprises an analysis of 37 cases[2] of ulcer of the stomach and duodenum in which a posterior retrocolic gastrojejunostomy had been made. In all of these cases the ulcer-bearing area had been excluded by the string method or by pyloric plication, or had been removed by local excision, pylorectomy, or partial gastrectomy. These latter are relatively few in number.

CLINICAL NOTES. The clinical symptoms following operation are of various kinds but fall naturally and readily into three classes:

Group A. The cases that do well after operation and have few or trivial symptoms. It has been found necessary to supervise carefully the postoperative diet of these patients in particular in regard to the curtailment of the amount of the alimentation. Under such a régime these patients are restored to health. There are 11 of these cases in the series.

Group B. This group includes those cases, 14 in number, in which, following operation, we were able to demonstrate a definite disturbance in the physiology of the stomach as exemplified in the secretory and motor functions. Clinically, the patients complain of definite dull, pressing, or cramp-like pain felt in the epigastric, substernal, or hypochondriac regions, and very often lower down in the perumbilical region or in the iliac fossæ. These pains are not identical with those felt before operation. They differ from the preoperative heartburn or from the colicky pain of pylorospasm. They are less severe, less definitely localized, and longer in duration. They often last throughout the whole or greater part of the digestive period. Vomiting is frequent; often it is repeated more than once daily after the taking of food; less frequently it occurs only once a day and then usually in the morning. The vomitus is not copious, and consists of sour biliary material. Food is frequently avoided because of the pain which it brings on.

[2] A few of the cases were originally operated upon while on the services of Dr. A. G. Gerster, Dr. A. V. Moschcowitz, Dr. C. A. Elsberg, and Dr. E. Beer. Some of the studies also were carried out while the patients were on the medical services of Dr. A. Meyer, Dr. N. E. Brill, Dr. E. Libman, and Dr. M. Manges. Our thanks are due to all of these gentlemen for their courtesy in permitting us to carry out these studies on their wards. We wish also to thank Dr. E. A. Aronson for the courtesy of permitting us to make some of these studies in the department of gastro-enterology of the dispensary.

The patient's weight may show some increase in spite of the gastric symptoms, but frequently an early increase is soon replaced by a loss.

The bowels are usually constipated, but occasional attacks of diarrhea may intervene.

Some degree of mental depression is frequently a pronounced symptom.

There are practically no physical signs; a moderate amount of diffuse epigastric tenderness is usual.

Group C. The third group is composed of cases in which mechanical disturbances in the function of the gastrojejunal stoma are present. There were 7 of these cases; 2 were instances of gastrojejunal ulcer and the remaining 5 of a gradually produced organic constriction of the stoma. The symptoms complained of were very similar to those in group B. The differentiation between groups B and C consists in the fact that in the former group there are functional disturbances and in the latter organic mechanical faults.

TABLE I.—CHEMISM OF THE STOMACH AFTER GASTRO-ENTEROSTOMY.

	Before operation.			1 to 4 months after operation.			4 to 12 months after operation.			1 to 4 years after operation.		
	Amt. c.c.	Free acid. %	Total acid. %	Amt. c.c.	Free acid. %	Total acid. %	Amt. c.c.	Free acid. %	Total acid. %	Amt. c.c.	Free acid. %	Total acid. %
Fasting stomach contents	45	..	..	33	9	28	33	9	19	20	15	27
Ewald test breakfast . .	74	47	72	127	27	61	148	37	54	190	32	60
Riegel test meal . . .	..	..	..	59	14	34	26	29	52	73	30	48

CHEMISM OF THE STOMACH AFTER OPERATION FOR ULCER. In discussing this phase of the subject we shall follow the same group classification as heretofore described. Considering first the 37 cases as a whole by reference to the chart (Table I) it will be noted that before operation the average fasting morning residue in the stomach is 45 c.c.; the average Ewald test meal residue (one hour after administration) is 74 c.c., with free acid 47 per cent. and total acid 72 per cent. During the first four months after operation it is to be noted that while the fasting residue has not increased (in fact it has diminished) the average amount of Ewald test meal removed is 127 c.c., free acid 27 per cent., total acid 61 per cent. We observe that the operation has actually delayed instead of hastened the motility of the organ. The acidity, however, is diminished though not to a considerable degree. In the period from four to twelve months after the surgical interference the same observation is made, namely, that the fasting content remains low while the Ewald test meal residue has now increased to 148 c.c., the individual acidities remaining as before. In the cases studied one to four years after operation a still greater delay in motility is

seen, the Ewald residue having increased now to 190 c.c., the acidities remaining the same.

In corroboration of this fact we have the figures for the residual amount removed six hours after the administration of a Riegel motor test meal. Before operation no residue; one to four months after, 59 c.c. can be removed, free acid 14 per cent., total acid 34 per cent.; four to twelve months after, 26 c.c., with moderately low acidities. One to four years after the amount removed after the Riegel meal has increased to 73 c.c., a distinctly abnormal amount, considering that the normal stomach should have completely emptied itself in the prescribed period. In considering these figures we must be forcibly impressed by the fact that gastrojejunostomy is after all not a drainage operation, that contrary to general opinion the emptying power of the stomach is not accelerated but is actually and truly retarded, due to factors to be considered later. This fact is further emphasized by a consideration of the chemism of the stomach in each of these three groups previously described (Table II). Group A, comprising cases apparently well and free of symptoms, shows, nevertheless, that the residue, removed one hour after the usual Ewald meal, is 113.8 c.c. (before operation 74 c.c.), to be regarded as an abnormally increased amount, since our standard for an Ewald meal in a well person is usually regarded as below 100 c.c. The acidity is slightly diminished. When we consider groups B and C, patients with abnormal symptoms after the surgical interference, we note that the returns from the Ewald meal in the second group, those with functional disturbances, is 156 c.c., while in group C those with organic stenosis of the stoma, it actually reaches 237 c.c., the acidities remaining about the same in all three groups. The Riegel motor meal shows an increase, though only a moderate one.

TABLE II.—POSTOPERATIVE CHEMISM ACCORDING TO GROUP DIVISIONS.

	Cases well.			Cases with functional disturbance.			Cases with anatomical disturbance.		
	Amt. c.c.	Free acid. %	Total acid. %	Amt. c.c.	Free acid. %	Total acid. %	Amt. c.c.	Free acid. %	Total acid. %
Fasting stomach contents	26	11	20	23	15	29	38	15	32
Ewald test breakfast	113.8	31	59	156	32	62	233	32	57
Riegel test meal	23	19	28	60	35	65	40	19	53

The results of the individual examination may be seen by reference to Tables III, IV and V. That the disturbance is one not only of motility but also of the secretory activity in the proportion of solid residue to the supernatant fluid in the test meals. While the usual normal proportion of solid to fluid is about 1 to 1, after operation the proportion rapidly becomes 1 to 4 even in the supposedly well cases, while in those with recurrent symptoms it averages 1 to 2, though in individual instances it may reach 1 to 5 or even 1 to 7.

TABLE III, GROUP A.—CASES WELL AFTER OPERATION.

Case No.	Roentgen ray.			Chemism.									Kymographic tracing.
				Fasting stomach contents.			Ewald test breakfast.			Riegel test meal.			
	Stoma.	Pylorus.	Peristalsis.	Residue. c.c.	Free acid. %	Total acid. %	Residue. c.c.	Free acid. %	Total acid. %	Residue. c.c.	Free acid. %	Total acid. %	Tonus contractions.
4	Patent and efficient	Closed 6 months postoperative	....	30	0	18	225 (S:F::1:2)[3]	24	54	..	..	..	Good.
10	Patent and efficient	Patent and efficient	Slow	30	4	10	70 (S:F::1:2)	50	86	No residue			Poor.
16	....	....	....	5	0	0	20	0	56	No residue			Fair.
17	....	....	....	75	22	40	150 (S:F::1:8)	50	71	70	58	83	Fair.
19	Patent and efficient	....	Good (no residue)	10	0	0	60	0	14				
22	....	....	....	25	10	22	75 (S:F::1:4)	16	46	..	..	..	Good.
28	....	....	....	30	18	32	60 (S:F::1:2)	62	86				
30	....	....	....	25	44	56	210 (S:F::1:20)	38	54				
33	....	....	....	5	0	0	40 (S:F::1:7)	74	86	..	..	..	Good.
38	....	....	....	..	..	..	28 (S:F::1:1)	8	50				
6	Patent and efficient	Patent and efficient	....	70	0	10	80	0	12	..	..	..	Good.
		Total	averages	26	11	20	113.8 (S:F::1:4)	31	60	23	19	28	

TABLE IV, GROUP B.—PHYSIOLOGICAL DISTURBANCES AFTER OPERATION.

Case No.	Roentgen ray.			Chemism.									Kymographic tracing.
				Fasting stomach contents.			Ewald test breakfast.			Riegel test meal.			
	Stoma.	Pylorus.	Peristalsis.	Residue. c.c.	Free acid. %	Total acid. %	Residue. c.c.	Free acid. %	Total acid. %	Residue. c.c.	Free acid. %	Total acid. %	
1	Patent; not efficient	Open after 6 months	Active; residue[4]	..	..	..	170 (S:F::1:2)	0	20	..	..	..	Fair.
2	Closed; not efficient	Open after 5 months	Residue[4]	25	10	22	230 (S:F::1:3)	38	63	..	..	..	Fair.
5	No evidence	Open after 10 months	Hyperperistalsis	90	46	48	300	44	64				
12	Very patent	Open after 5 months	....	16	10	25	160 (S:F::4:1)	11	45				
11	Inefficient	Open after 2 months	Active; residue[4]	65	21	41	125 (S:F::2:3)	36	68	..	..	..	Fair; poor.
15	....	....	....	50	0	15	150 (S:F::1:3)	30	50				
21	Inefficient	Open	Very active; sl. residue[4]	15	0	24	20 (S:F::1:1)	28	60	..	..	..	Poor.
25	Efficient	Open (no exclusion)	Hyperactive; no residue	25	18	31	70	32	94	35	36	62	Fair.
27	Efficient	Open after 4 months	Very active; no residue	18	40	54	50 (S:F::2:3)	52	92	50	46	86	
32	....	....	....	25	12	30	60	16	65	40	14	30	Fair.
35	....	....	....	..	..	..	150	74	95	70	80	94	Fair.
39	....	....	....	..	..	..	200	17	48				
9	Inefficient	Open	Residue[4]	1	0	0	350	14	51	100	0	55	
		Total	averages	23	15.7	27	156 (S:F::1:2)	30	62.6	60	35	65	

[3] This refers to the proportion of solid to fluid ingredients in the test meal.
[4] = after six hours.

TABLE V, GROUP C.—ANATOMICAL DISTURBANCES AFTER OPERATION.

Case No.	Roentgen ray			Chemism.									Kymographic tracing.
				Fasting stomach contents.			Ewald test breakfast.			Riegel test meal.			
	Stoma.	Pylorus.	Peristalsis.	Residue. c.c.	Free acid. %	Total acid. %	Residue. c.c.	Free acid. %	Total acid. %	Residue. c.c.	Free acid. %	Total acid. %	
3	....	....	....	00	12	46	90	24	66	27	0	73	
							(S:F::1:2)						
13	No evidence	Open after 2 months	Violent residue[6]	44	8	21	190	30	64				
14	Inefficient; no evidence	Open after 1 year	Violent residue[6]	60	27	54	450	30	50	..	..	..	Good.
							210	34	52	..	..	..	Fair.
							(S:F::2:1)						
18	Patent inefficient	Open	Hyperperistalsis; residue[6]	50	27	41	200	30	53	..	..	..	Poor.
24	Inefficient	Open	Excessive activity	10	0	0	600	33	50	30	0	18	Good.
26	....	....	....	5	..	..	230	33	64	70	30	50	Fair.
							(S:F::1:5)						
27	....	....	....	..	..	..	20	17	35	50	46	86	
34	....	....	....	..	..	..	105	42	77	30	22	36	
		Total averages		38	15	32	233	32	57	40	19	53	
							(S:F::1:2)						

This is to be interpreted as an increase, often very marked, in the outpouring of gastric secretion, a hypersecretion associated with the

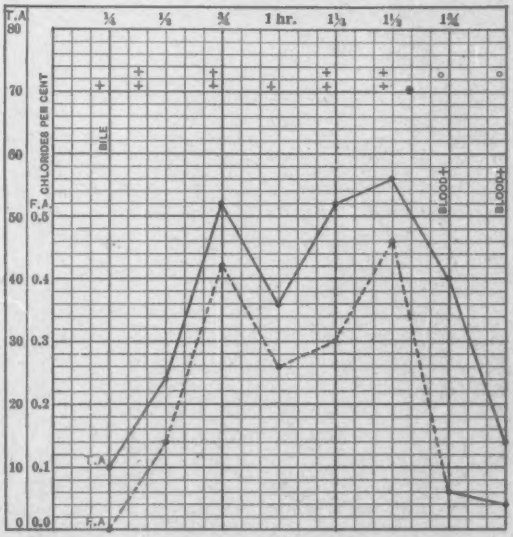

FIG. 1.—Gastro-enterostomy with string exclusion. Cured case.

delayed motility. The quantity of liquid residue removed often exceeds the amount of fluid actually administered in the test meal.

[6] = after six hours.

Our efforts further to elucidate the problem of gastric secretion after radical interference led us to adopt the method of fractional estimation of stomach contents as demonstrated by Rehfuss. Thin oatmeal water was utilized as the test substance and estimations made of the acidity of the stomach every fifteen minutes. This non-solid test substance is much more simple than the Ewald or Riegel foods, and gives slightly lower figures for the strength of acid secreted. With this test the cases in group A show a prac-

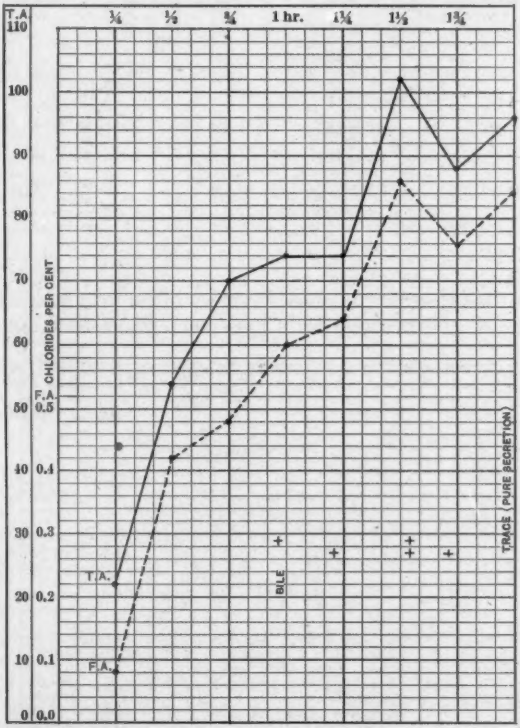

FIG. 2.—Gastro-enterostomy with exclusion by pyloric plication. Case with functional disturbances.

tically normal curve (Fig. 1), the acidity mounts gradually to the third period (three-quarter hour), then drops abruptly, due to the inflow of regurgitant intestinal contents, as evidenced by the admixture of bile; it then has a secondary rise lasting to the sixth or seventh period (one and one-half to one and three-quarter hours), following which the acidity diminishes as the end of the period of digestion approaches. The groups B (Fig. 2) and C (Fig. 3) follow the same course for the first five or six periods, but exhibit later a more prolonged and sustained secondary rise, lasting occasionally

to an eleventh or twelfth period (two and three-quarter to three hours) before the stomach is completely emptied. In these latter groups the acidity most frequently remains high to the end of digestion, never approaching the base line. In group B those cases with inefficiency of the stomach from functional causes the regurgitation of bile begins earlier and is greater in amount; the group of organic stenoses showed diminished intestinal regurgitation.

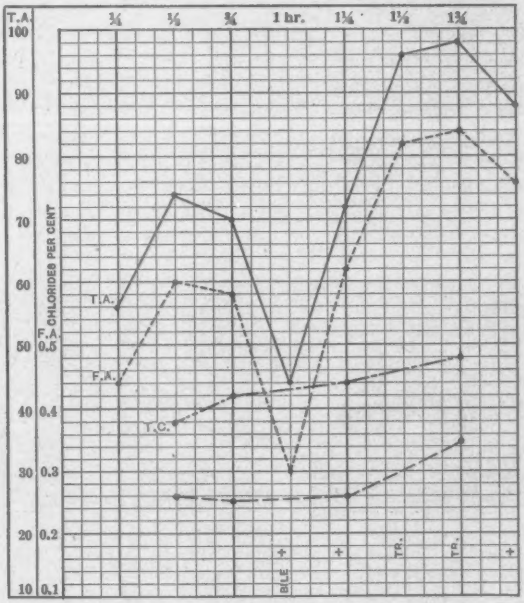

FIG. 3.—Gastro-enterostomy with string exclusion. Case with anatomical disturbances.

THE MECHANICS OF THE GASTRIC MUSCULATURE AFTER OPERATION. We have spoken often in this paper of the retardation of gastric motility. It is our contention that the delay in the emptying power of the stomach is due less to diminished peristaltic activity of the organ and more to diminution in the tone of the stomach wall (peristolic tone) and improperly coördinated muscular contractions. That an atonic and dilated stomach can still show vigorous contractions is generally conceded by all radiographers. That such is the condition after gastrojejunostomy we are able to demonstrate by two means: (1) by kymographic tracings of the empty stomach, and (2) by radiographic studies with the aid of the usual contrast meal.

The technic adopted by us for kymographic tracings is essentially that employed by Cannon and Washburn and Carlson and his collaborators in their well-recognized physiological studies of the

motor mechanics of the stomach wall of men and dogs. In the fasting state the patient is requested to swallow a small rubber balloon to which is attached a narrow-bore rubber tubing about thirty-six inches long. The efferent end of this tubing is attached by a T-shaped connection to both a mercury manometer and to a needle (by means of a tambour), which records on a slowly revolving drum the variations in intragastric pressures. Tracings are taken for one-half to three-quarters of an hour. The results obtained by this method of study of the peristolic tone of the stomach in the fasting state are most interesting and instructive. The normal stomach (Fig. 4) gives evidence of slow tonal contractions in its fasting state; these contractions follow each other quite regularly, the wave itself enduring for thirty to forty seconds, with a period of quiescence between contractions of usually thirty seconds. These are not peristaltic waves but are variations in the constant peristolic tonal state of the resting organ. A second type of contraction, the so-called hunger contraction (Fig. 5), is demonstrable in addition

FIG. 4.—Exploratory laparotomy; no lesion found. Upper curve indicates tracing of muscular activity; lower one is the respiratory curve taken from the abdominal wall. Time marked in minutes.

in every normal stomach. These are stronger and more vigorous as well as more rapid contractions, lasting twenty to twenty-five seconds, with a quiescent state of twenty to thirty seconds between each wave. These latter contractions are more variable in their appearance, occurring singly or more usually in groups of two or three contractions. At other times they are vigorous and rapid and may last continually for almost half an hour. We are able to confirm the statement of Cannon that hunger contractions are an indication of the freedom of the stomach from organic disease. The smaller but more constant contractions are an evidence of the tonal variations in the gastric peristole, and bear an important significance for our study.

Turning now to a consideration of the kymographic tracings of diseased stomachs we note that cases of gastric neurosis of some type and vagotonia (Fig. 6) show markedly increased tonic contractions and exaggerated and rapid hunger contractions. On the contrary, those cases of atonic and prolapsed organs show dimin-

ished tonal waves and often absent hunger contractions. In our series, cases of gastric or duodenal ulcer have with only one exception failed to give evidence of hunger contractions. The tonal

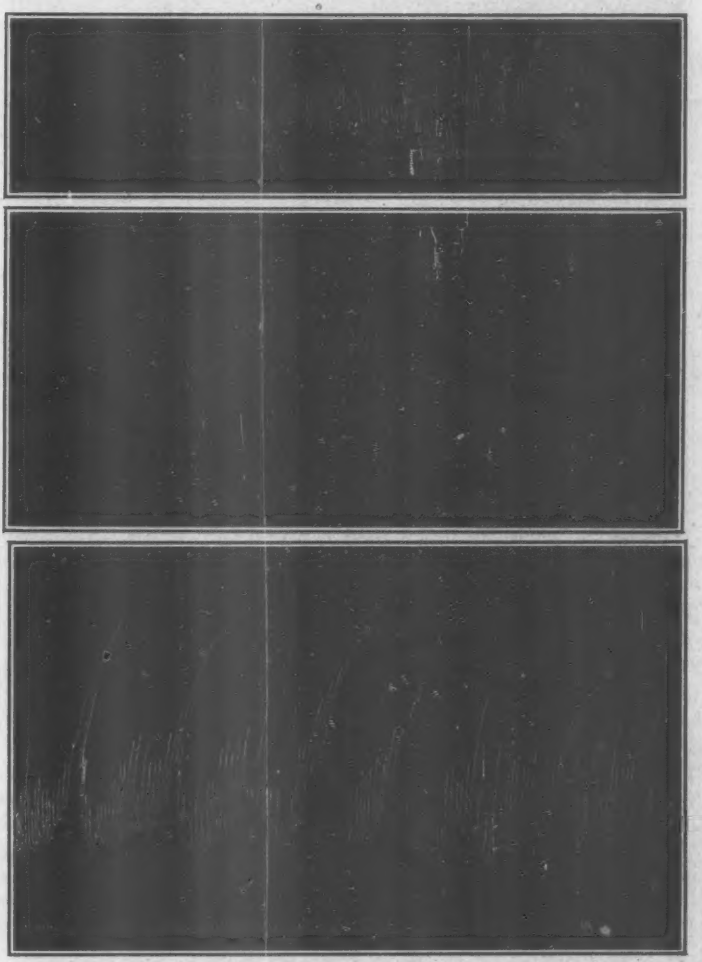

FIG. 5.—The same as Fig. 4. The three parts form a continuous record.

waves are retained though often of an irregular and discoördinated variety. Before operation there is no evidence of diminished tone, with the single exception of a case of penetrating ulcer of the lesser curvature in which reflex pylorospasm and inhibition of motility

produced dilatation of the organ; in this case all evidence of any contraction was absent.

Let us now compare the kymographic tracings of cases after operation with the ante-operative curves. We will note that almost all the cases examined within one month after the radical procedure show a complete loss of the peristaltic function of the organ; the curve becomes almost flattened out, a few irregular contractions being present in a smaller percentage of cases. In group A the cases that have become well, 3 cases out of 7, show already good tonal contractions as well as very good hunger contractions shortly after the surgical procedure; a fourth person regains his contractions some time later; 3 of the cases to date have evidenced some sign of returning tonal waves, but as yet no hunger contractions. In group

FIG. 6.—Exploratory laparotomy; no lesion found. Diagnosis: vagotonia.

B the cases classed by us as examples of functional disturbance, of 8 cases traced, 4 show poor or no tone (Fig. 8) and 4 only fair tonal contractions. There is no single instance of the more vigorous hunger contractions in this group. As a control we give Fig. 9, which shows the character of tonal wave and hunger contractions in the stomach of a man upon whom exploratory laparotomy had been performed and no disease found.

In group C those cases of organic stenosis of the gastrojejunostomy stoma, of 4 cases traced, 2 retained good and 2 retained fair tonal waves. Hunger contractions are again absent, though we note that none of them can be classed as having poor or absent tonal contractions (Fig. 10).

Thus we see that group B is characterized by the presence of

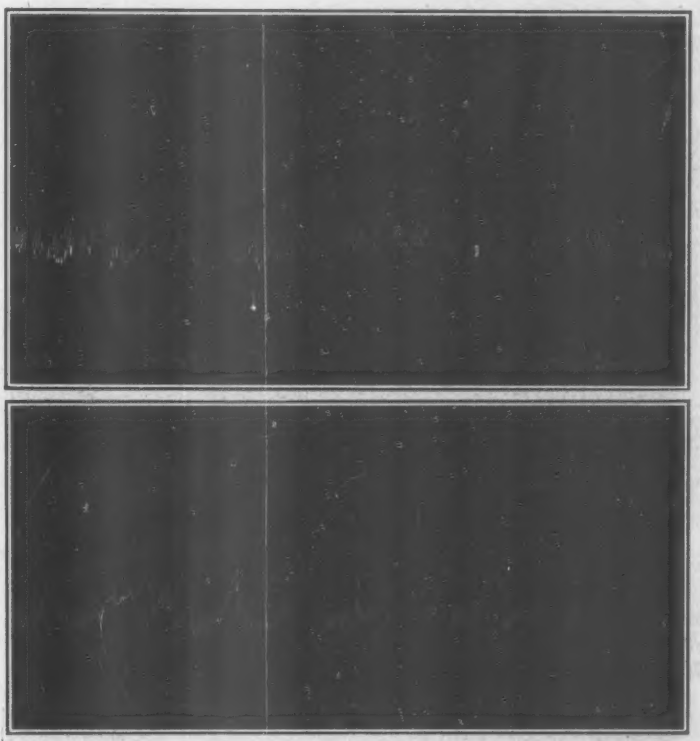

FIG. 7.—Gastro-enterostomy with pyloric exclusion by the string method. Six months after operation; cured case. Type of curve customarily seen in patients having no lesion in the stomach. The two parts form a continuous record.

FIG. 8.—Gastro-enterostomy with pyloric plication for duodenal ulcer. Two years after operation; functional disturbances.

only poor or fair tone, and the complete absence of any example of good tonus or hunger contractions. Group A shows fair tone soon after the operation and a regain of normal tone soon after or later after the surgical procedure; it is in this group of practically

FIG. 9.—Exploratory laparotomy; no lesion found. One month after operation; demonstrating non-interference with the muscular activity of the stomach when the latter is only handled and when no operative procedure is carried out. Compare with Fig. 5 which represents a tracing from the same stomach before operation.

well cases that we see the only return to the normal condition of hunger contractions (Figs. 11, 12, 13, and 14). The organic stenosis cases (group C) retain fair tone but never show hunger waves. Thus, all in all of the 17 cases traced after operation 11 showed definite diminution of tone; only 6 retained good tone.

FIG. 10.—Gastro-enterostomy with string exclusion. One year after operation; secondary operation showed narrowing of the stoma and slightly patent pylorus. Curve illustrating muscular activity in the presence of an anatomical obstruction to the egress of the stomach contents.

RADIOGRAPHIC EVIDENCE. This may be summarized as follows: In those cases in which there is return to health (group A, Table III) (11 out of 37) peristalsis is noted as good; there is no residue six hours after the administration of the contrast meal; the stoma is reported as open and functionating efficiently. In the second group (group B, Table IV) those with disturbances of the muscular tonal mechanism as well as of secretory activity the stoma is mentioned

as inefficient in 5 instances of 9 examined, in a sixth case as completely non-functionating. In the other 3 cases the stoma is spoken of as efficient by the contrast meal method of examination. In all of these cases the pylorus is shown to have reopened in spite of

FIG. 11.—Case of duodenal ulcer before operation.

the string exclusion, the earliest case examined being two months after the operative procedure. In all of the instances the peristalsis is described as active or very active, yet in 5 of the 8 cases a bismuth residue is noted after six hours. In the final group C, table V of

FIG. 12.—Same case as Fig. 11. Four weeks after operation. Kymographic tracing showing almost complete absence of tonus changes and complete absence of hunger contractions.

organic stenosis of the stoma, the stoma is described 3 out of 4 times as inefficient and once as completely obliterated; the pylorus is open in all the cases, only partly open in half of them. Peristalsis is observed three times as violent, once as hyperactive.

In recapitulating the dominant characteristics of these three

groups obtained by the various means at our disposal we will recall the following: 37 cases have been examined to ascertain the functional activity of the stomach after gastrojejunostomy as performed by competent surgeons employing a technic uniformly accepted today.

FIG. 13.—Same case as Figs. 11 and 12. Five weeks after operation showing beginning return of tonus contractions and at one point an incomplete attempt at a hunger contraction.

Eleven of these fall into group A. These have all been regarded as well. Clinically they have few trivial or no complaints. Chemical examinations demonstrate a mildly diminished motility after Ewald and Riegel test meals, with diminished acidity and a moderate

FIG. 14.—Same case as Figs. 11, 12 and 13 now four months after operation. Note the return of the regular tonus contractions of the gastric musculature as also the presence of hunger contractions though not yet in full strength.

but distinct and persistent hypersecretion. The fractional method of Rehfuss shows a nearly normal curve. Kymographic tracings show moderate diminution in the tone, but in about half of the cases a return to the normal occurs very soon. The roentgen ray fails to show a six-hour residue and the stoma functionates properly.

The next 14 cases fall into group B. These cases remain poorly nourished and complain of the following symptoms: pain, vomiting, occasionally hematemesis, constipation, or rarely diarrhea. They are frequently depressed mentally. Chemically, definite delay in motility is shown and hypersecretion is present. The stomata functionate poorly. The kymograph shows either a complete absence or a marked diminution of the peristolic tone and the normal hunger contractions are not regained The radiograph shows the stoma to be functionating improperly and the peristalsis is noted as active or very active. This group is characterized mainly by disturbed muscular function leading to inefficiency of a still patent stoma with definite delay in gastric motility.

The third group comprises 7 cases of organic stenosis of the stoma. Clinically, they resemble the preceding group. Chemically, they show even a greater degree of gastric retention and delayed motility. By the kymograph they may be shown to have regained fair or good peristolic tone. Radiographically, they show violent peristalsis, six-hour residues, and inefficient or closed stomata.

Discussion. The foregoing study must tend to cause us to reconsider our views as to the events taking place after operative procedures upon the stomach. It becomes evident that the impression now very generally in existence that gastrojejunostomy is an operation which in no way impairs the functional efficiency of the stomach is an erroneous one. The operation leaves this organ definitely impaired in a large percentage of the cases. The creation of a new opening in a situation not intended by nature disturbs the peristolic tone of the stomach, the secretory function, and the nervous mechanism controlling both. In only a minority of the cases does the stomach return to an almost normal state of functional activity.

How great a factor artificial pyloric exclusion plays in this disturbance we cannot estimate with any degree of accuracy, though we may suspect it of playing some role. It is well known that the best results after operation have been obtained in cases in which some pathological process has gradually caused a stenosis at the pylorus. Here conditions have been prepared over a long period of time for the proper functioning of an artificial stoma, and when made it acts immediately as a long-sought-for and much-needed exit. The sudden artificial attempt to imitate this causes an uncoördinated muscular activity directed in an improper fashion and is perhaps accountable for at least part of the disturbances seen after such operations.

We must plead with the surgeon sedulously to avoid what has so aptly been called by v. Eiselsberg a "concession operation," by which we understand a gastrojejunostomy in cases in which no definite organic lesion is demonstrable in the stomach at operation. These are the cases which show the greatest amount of disturbance

of function after operation. These cases as well as all doubtful cases ought to be relegated to the medical man, who if he cannot always show the brilliant successes of the surgeon, will by his diligence preserve the patient from some of the unpleasant sequelæ which can readily arise after even a well-judged operation.

We express our appreciation to Dr. A. A. Berg, the head of the gastro-enterological service, for his many courtesies during the course of this work.

This paper is not intended to indicate in any way the percentages of total or partial cures or of recurrences of some or all of the symptoms after operation. The apparent emphasis put upon those cases with recurrent symptoms after operation was purposeful, in that we aimed particularly to investigate the causes for the recurrence of symptoms after operation.

TWO CASES OF PROBABLE SYPHILIS OF THE INTESTINES.

By D. A. Haller, M.D.,
and
I. C. Walker, M.D.,
Boston.

(From the Medical Clinic of the Peter Bent Brigham Hospital, Boston.)

Approximately 700 cases of syphilis have been under observation either in the wards or in the Outdoor Department of the Peter Bent Brigham Hospital during the past three years. Although a number of these cases have presented interesting lesions, the two cases which we report in this paper we believe to be very unusual. In this series of 700 cases there were 14 individuals who showed lesions of or symptoms referable to lesions of the alimentary tract. This is exclusive of early cases with mucous patches in the mouth and throat and similar lesions about the anus, and also exclusive of those cases, with positive findings in the spinal fluid, having gastro-intestinal symptoms which were due to neurological conditions. Of the 14 cases mentioned above, 9 showed syphilitic lesions recognized as being common: gumma of the tongue 4, gumma of the palate 3, stricture of the rectum 2. In two other cases the gastro-intestinal symptoms were possibly due to syphilis. One, a woman, three months pregnant with a ++++ Wassermann reaction, complained of persistent vomiting which cleared up with rest in bed, light diet, and two doses of salvarsan. A second case with a ++++ Wassermann reaction complained of pain and burning in the epigastrium and had a positive guaiac test in the stools. Operation disclosed nothing in the stomach or duodenum which would explain the symptoms. She

was given no antisyphilitic treatment, and it has been impossible to get in touch with her since she left the hospital. What influence, if any, syphilis had in these two cases it is not possible to say. Another case with a ++++ Wassermann reaction complained of vomiting and loss of weight, and bismuth roentgen-ray examination suggested carcinoma of the stomach. Under intensive antisyphilitic treatment for one month the patient gained in weight, but as repeated bismuth roentgen-ray studies showed no change in the stomach, laparotomy was done. A diagnosis of syphilis of the stomach was made at operation. The remaining two cases of the group of 14 we will consider in detail as probable cases of syphilis of the intestines.

CASE I.—J. P. N. Medical No. 25. White; male; single; born in Ireland thirty-two years ago. Entered the hospital April 14, 1913, complaining of bloody diarrhea.

Family History. One sister died of pulmonary tuberculosis seventeen years ago. Just before her death she developed a bloody diarrhea. A second sister died of pulmonary tuberculosis thirteen years ago. A third sister died of the same condition seven years ago and developed a bloody diarrhea before death. An only brother died of pulmonary tuberculosis three years ago. Patient was not immediately exposed to infection from any of these cases. Father is living and well. Mother died seven years ago after an operation for intestinal obstruction.

Past History. Patient has not lived outside of the New England States and New Brunswick, Canada, since he came to America, twenty-five years ago. He has always worked as a harness-maker. He uses alcohol to excesss and periodically gets drunk. He had scarlet fever in youth, but gives no history of tonsillitis, rheumatic fever, chorea, pleurisy, pneumonia, malaria, or serious injury. He has had gonorrhea three times; the last attack was four years ago. Fourteen years ago, without any previous local lesion, he had a rash which covered his face, body, and hands. There was no itching. A few days later he developed sores in his mouth and a sore throat. He was treated with mercury by mouth for four months, but has had no antisyphilitic treatment since. Twelve years ago he was treated at Rutland, Mass., for pulmonary tuberculosis. During the five months there he gained 47 pounds in weight. He is not sure, but thinks that tubercle bacilli were found in his sputum on one examination. After leaving Rutland he went down to his former weight of 140 pounds and has remained at that figure up to the present illness.

Present Illness. Duration seven years. In the summer of 1906 he developed a bloody diarrhea averaging ten to eleven bowel movements daily. These were very loose and bright yellow, and were mixed with dark blood at times and often covered with bright, fresh blood. At various times he passed pure blood alone and small strings of mucous membrane with the blood. The first attack of these

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symptoms lasted three and a half months. There were severe griping pains in the abdomen, worse before and just after defecation. He lost 7 pounds in weight. The attack passed off gradually. He had an attack of the same character of only three days' duration during the following winter. The next summer, 1907, he had a second severe attack which lasted two and a half months, during which he lost 3 pounds. The following winter he had a third severe attack of five months' duration. During this attack he went to the Bar Harbor Hospital, where he remained three weeks, and under a restricted diet and medicine by mouth the symptoms gradually cleared up. Since that time, six years ago, he has had repeated attacks which come at intervals of about six months, and which last from six to eight weeks. The present attack began six months ago and has been similar to those described above, except that it was more severe. In the last two weeks he has lost 10 pounds in weight. He has no cough, raises no sputum, has no cardiac or renal symptoms, and no neurological disturbances, except that he is nervous about his present condition.

Physical Examination. Temperature 98.6°, pulse 80, respiration 22. Patient is a well-developed and fairly well-nourished man lying flat in bed and apparently comfortable. Skin: negative except for slight acne over shoulders and back. Glands: epitrochlear, cervical, and inguinal; are palpable, but not markedly enlarged. Eyes: an irregular corneal scar due to trauma causing an irregular and fixed pupil is present on the right; the left pupil reacts to light and accommodation. Tongue, teeth, and mouth are essentially negative. Thyroid not enlarged. Chest is long and narrow, with some flattening of the right side anteriorly. Lungs: negative findings. Heart: negative findings. Pulses: equal and regular. Blood-pressure: systolic 130, diastolic 60. Abdomen: in the lower right quadrant the individual loops of intestine are easily made out through the belly wall and are slightly tender to firm pressure. No masses are felt. Liver not enlarged and the edge is not felt. Spleen not felt. Extremities negative. Reflexes: deep and superficial are present and equal on the two sides.

Laboratory Examinations. Urine: clear; acid; specific gravity 1018; no albumin; no sugar; sediment negative. Blood count was as follows: hemoglobin 70 per cent., white blood cells 12,200 per c.mm., polynuclear neutrophiles 57 per cent., lymphocytes 38 per cent., eosinophiles 5 per cent. Wassermann reaction ++++. Spinal fluid: cells 2 per c.mm.; globulin (Noguchi) negative; positive Fehling's test; Wassermann reaction negative. Stool examination showed blood and pus mixed with much mucus; no food residue. Many examinations failed to show amebæ, tubercle bacilli, ova, and parasites. Guaiac test was strongly positive.

Bismuth Roentgen-ray Examination. No evidence of gastric or duodenal ulcer; some ileal and cecal stasis, a bismuth residue in the

ileum after nine hours and in the cecum after thirty hours. Roentgen ray of chest: no evidence of tuberculosis. There is a slight increase in the density of the shadow around the root of the right lung.

Proctoscopic Examination. There is considerable tendernesss on insertion of the proctoscope and marked pain on slight inflation. Nothing abnormal seen at the sphincter margin. The mucous membrane of the rectum is definitely hyperemic and there is a surface coating of bloody purulent mucus which can be wiped off, leaving a granular looking surface epithelium which shows evidence of some superficial desquamation. There are no discrete circumscribed ulcers made out, but there are numerous small hemorrhages in the mucous membrane. Apparently the rectal wall is thicker, firmer, and more rigid than normal, and gives one the impression of a leathery consistency. The longer sigmoidoscope reveals much the same condition in the lower sigmoid. Smears made from the wall of the bowel are negative for tubercle bacilli.

For approximately three weeks the patient's condition remained as at entrance. Stools similar to the admission specimen were passed from six to eight times daily. Temperature continued normal; pulse averaged 70; respirations 20. Irrigating fluids were varied from warm normal salt solution to 1 to 1000 silver nitrate. Patient stated that all of these irrigating fluids and many more had been tried in previous attacks without effect.

Three weeks after admission, treatment with neosalvarsan was begun. In the week following the second injection the stools averaged two daily, and were yellow brown with an excess of mucus. Occasionally fecal masses were found with some undigested food and occasional streaks of blood. Examinations for tubercle bacilli done approximately twenty times were always negative. Neosalvarsan was continued at weekly intervals.

June 3, seven weeks after admission and one month after the first dose of neosalvarsan, proctoscopic examination was repeated by the same observer. Mucous membrane of the lower rectum reveals a thin coating of pinkish-brown mucus which can be easily wiped away. The underlying mucous membrane is less hyperemic than on previous examinations, but the surface is still somewhat granular in appearance. There are no definite ulcerations. The small punctate hemorrhages that were seen before have disappeared. On the whole there has been marked improvement. The mucous membrane is less injected and less roughened. No free blood is present anywhere. The tenderness and discomfort after the previous examination were not noticed this time.

Patient was discharged from the hospital June 9 after a total stay of fourteen weeks. During the last three weeks he averaged only one movement a day. Improvement in his general condition was marked. He gained weight, his appetite improved, and he felt stronger and better in every way, and had no discomfort on going to

stool. Hemoglobin rose from 70 to 90 per cent. A stool examined on the last day of his stay in the hospital was large, well formed, dark brown, without mucus or blood; microscopic examination negative; guaiac test faintly positive. The total amount of neosalvarsan given was 4.2 grams.

For eight months after leaving the hospital the patient was lost track of. A letter was received from him February 3, 1914, saying that symptoms of his former trouble were reappearing. He was readmitted February 28, 1914. At this time he stated that for six months after leaving the hospital he was perfectly well. About Christmas he noticed a beginning frequency of defecation, which rapidly grew worse. Blood began to reappear in his stools, and he noticed severe griping pain in the lower abdomen. At present he is having eight to ten movements daily. He is weak, tired, somewhat worried and nervous, has many headaches, and does not sleep well. Physical examination shows no points of difference from that of first admission. Stool: brown; semifluid; no parasites or ova; slight amount of mucus and few blood streaks; no tubercle bacilli. Wassermann reaction ++++ in the serum.

Sigmoidoscope Examination. Slight tenderness on insertion and very little pain on inflation. There is a great deal of mucopus and free blood in the lumen of the bowel, and the mucous membrane everywhere seems coated with the same material. This is readily wiped away, leaving a very injected granular surface which shows many punctate hemorrhagic spots and bleeds at a touch. There are no definite ulcers.

Bismuth Enema and Roentgen-ray Examination. Examination of the colon shows a normal configuration of the cecum, ascending colon, transverse colon, splenic flexure, sigmoid flexure, and rectum. The lower aspect of the descending colon shows abnormal findings. The bismuth enema stops for a few minutes on reaching this point, afterward it passes the descending colon abnormally quickly and no complete filling of this part of the colon can be demonstrated. This is very likely due to spastic contractions of the wall of the descending colon. The upper portion of the descending colon as well as the rest of the colon shows a broad normal filling. The enema does not pass the ileocecal valve. Bismuth given by mouth shows a normal transport as far as the upper portion of the colon. After three days, in spite of several movements, a definite stasis in the descending colon is seen.

Salvarsan, 0.3 gram, was given March 3. No improvement resulted in the number or character of the stools during the next ten days. A second dose of 0.5 gram was then given, and almost immediately the number of stools per day fell to two, and on March 18 the stool is described as formed, brown, streaked with blood, with a small amount of mucus. Guaiac test positive. Bismuth roentgen-ray examination was repeated March 21. About

fourteen hours after the bismuth meal a complete filling of the cecum, the ascending and transverse colon is to be seen as far as the splenic flexure. There is no evidence of stasis at the upper portion of the descending colon, as on previous examination. In the middle of the descending colon, however, one haustrum shows an unusual amount of gas. The examination the following day shows a considerable amount of bismuth scattered out in the entire colon. There is a considerable amount of gas to be seen in the descending colon. A bismuth enema fills the entire colon as far as the cecum without any hindrance. He left the hospital at the end of a three weeks' stay, but was readmitted several times during the following weeks for additional salvarsan treatment, staying in the hospital for only twenty-four hours. The salvarsan given totaled 4.8 grams. The last dose was May 23, 1914. He was again seen October 23, 1914, at which time he reported that he was perfectly well. On one or two days he had had loose movements, but he had passed no mucus, pus, or blood. June 20, 1915, a letter was received from St. Johns, N. B., where he now lives: "I am in good physical condition, working thirteen hours a day. My weight is within 4 pounds of normal. One month ago I had an attack of diarrhea lasting about one week and passed fresh red blood and undigested food, but this soon cleared up without any treatment. At times feces when very firm are ribbon-shaped and are passed with difficulty. This does not seem to be growing worse."

Differential Diagnosis. In this case we believe that malignant disease can be ruled out on the duration alone, eight years. The diagnosis evidently lies between syphilis and tuberculosis. The latter we have discarded as a probability because of the absence during the three years while under our observation of all signs of active tuberculosis elsewhere either by physical or roentgen-ray examination; the absence of signs of active tuberculosis elsewhere on repeated physical examinations at other hospitals; sputum always negative for tubercle bacilli; absence of fever, rapid pulse, and night sweats; loss of weight was always proportional to the diarrhea; stools were always negative for tubercle bacilli; smears made directly from the wall of the bowel were negative for tubercle bacilli on three occasions; extreme chronicity.

We consider it proved that the patient has syphilis because of the history of infection, the general adenopathy, and the persistently strongly positive Wassermann reaction. We also believe the condition to be syphilitic because of the tendency to spontaneous healing, the distinct improvement locally, and in the general condition of the patient following neosalvarsan the relapse followed by definite and more lasting improvement under salvarsan, inefficacy of other forms of treatment, present excellent general condition of the patient, and the absence of symptoms of local active disease.

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CASE II.—R. D. A. Medical No. 3486. Negro; male; single; born in North Carolina twenty-nine years ago. Admitted to the hospital October 19, 1915, complaining of stomach trouble.

Family History. Father, mother, six brothers, and three sisters are living and well. Three sisters died in infancy of unknown cause. No history of hereditary or contagious diseases in the family.

Past History. Patient worked as a machinist up to six years ago; since then he has worked as a hotel waiter. He had measles, mumps, whooping cough, and occasional attacks of tonsillitis as a child. There is no history of other diseases or of any injury. No cardio-respiratory symptoms. Ten years ago he had two attacks of severe vertigo which lasted three or four minutes, but has had none since. There have been no neuromuscular symptoms, no fainting spells, spasms, disturbances of sensation, ataxia, girdle, shooting or muscle pains. He had gonorrhea four years ago, followed by no complications. Six years ago he had a hard genital chancre which was treated with mercury by mouth. There was no rash, no sore throat or sore mouth, and no loss of hair following this primary lesion. One year ago he had an enlarged inguinal gland which was opened and drained at this hospital. Nine months ago his best weight was 185 pounds, and he lost no weight up to the onset of the present trouble. Appetite was always good and he could eat anything. Bowels were usually regular. He never had nausea, flatulence, vomiting, hematemesis, colic, jaundice, diarrhea, or abnormally colored stools. During the past year he has had some trouble from external hemorrhoids.

Present Illness. Two weeks ago, while going home from work, he suddenly became nauseated and vomited. The vomitus was not of large amount or dark colored, and contained no blood. He had no pain at any time. During the next few days he continued to work, but he vomited once or twice daily. Three days after the first attack of vomiting he noticed colicky pain in the epigastrium; this pain did not radiate and was not related to meals, but was worse between 6 and 8 P.M. and between 2 and 3 A.M. The pain was not relieved by food, and no food would stay down. He had considerable belching of gas, which was partially relieved by soda and ginger. One and a half weeks ago he gave up work and went to bed. In a few days the pain and vomiting ceased and he went back to work. Two days ago the pain and vomiting recurred, forcing him again to stop work. During the last day the vomitus was black in color. He was markedly constipated. His stools have not been of abnormal color. He has had no chills or fever, no cough, dyspnea, edema, or palpitation.

Physical Examination. A well-developed but poorly nourished young negro lying comfortably in bed. Skull, scalp, and skin show nothing of interest. Eyes: pupils are equal and regular, reacting well to distance. To light they sharply contract and then dilate.

There is no photophobia, lacrimation, nystagmus, ocular palsy, lid lag, or exopthalmos. No disturbance of vision. Ears: deafness on the left side, normal hearing on the right. Mouth: marked pyorrhea; no ulcerations and no bleeding. Glands: epitrochlears are palpable on the two sides; several cervical glands are palpable in the posterior triangles; the inguinals are palpable on both sides, and there is a healed scar of an old incision for bubo on the left. Thorax is well developed and symmetrical, with good and equal expansion on both sides. Lungs: good resonance and fremitus and normal breath sounds throughout. Heart: no abnormalities are made out in size, impulse, or sounds. Blood-pressure: systolic 106, diastolic 68. Abdomen is symmetrical, level, and tympanic throughout. No masses are felt. There is slight tenderness on palpation in the epigastrium. Upper border of the liver is at the fifth rib; the edge is not felt. Spleen is not palpable and not enlarged to percussion. Kidneys are not felt. Reflexes: palate reflex is present, the cremasteric and abdominal are greater on the right than on the left. The biceps, triceps, radioperiosteal, knee, and Achilles reflexes are not obtained on either side. There is failure to bring the forefingers of the hands together accurately with the eyes closed, but the finger-to-nose and the heel-to-knee tests are well performed. There is no ankle clonus and no Kernig sign present. Gordon and Oppenheim reflexes are negative. Romberg test slightly positive. Sensation is nowhere impaired. Rectal examination: no hemorrhoids; no stricture; prostate is not enlarged or tender; no masses are felt and there is no blood on the examining finger. Temperature 98°, pulse 80, respirations 20. Weight 70.6 kg.

Laboratory Examination. Urine: amber; acid; clear; specific gravity 1029; no albumin; no sugar; no acetone; no diacetic acid; no bile present. The sediment is negative. Blood: hemoglobin 92 per cent., white blood cells 7300 per c.mm. Polynuclear neutrophiles 77 per cent., lymphocytes 23 per cent., no eosinophiles and no basophiles seen. Red blood cells 5,000,000 per c.mm. Wassermann reaction ++++. Spinal fluid: clear; 8 lymphocytes per c.mm.; globulin (Noguchi) negative; positive Fehling's test; Wassermann reaction negative with 2 c.c. Stool: dark, tarry, and soft; several large masses of mucus are present. Guaiac test is positive. Microscopically many red and white blood cells are present, no ova and no ameba found. Vomitus: 100 c.c. of dark brown material with gross food particles and much mucus; guaiac test positive. Gastric contents on fasting: 70 c.c. of greenish-yellow fluid with some well-digested food residue and much mucus. Microscopically a few red blood cells and epithelial cells and some starch and fat noted; no sarcinæ or Boas-Oppler bacilli found. Free HCl absent, total acid 22; guaiac test positive. Test meal (Ewald one hour): 100 c.c. of a pale green fluid with much well-digested food residue but no mucus. Guaiac test negative. Microscopically much starch and fat.

Roentgen-ray Examination. Standard bismuth meal given at 6 A.M. At 10.30 a large trace remained in the stomach, the lower ileum was filled and a small amount was present in the ascending and transverse colon. After a special mixture of malted milk, corn starch, and 90 grams of bismuth subcarbonate the stomach was negative; the pylorus and duodenum were regular in outline. At 9.30 A.M. the following day there was a small residue in the terminal portion of the ileum, indicating ileal stasis; the larger part of the residue was in the descending colon. At 12.30 on the third day a bismuth enema showed the sigmoid to be very redundant, one loop reaching the height of the splenic flexure. When completely filled the splenic flexure was parallel with the descending colon. Roentgen-ray of the chest showed negative findings.

For two days he was given cracked ice and small amounts of milk. Bismuth studies were begun on the fourth day and lasted for three days, as noted above. October 24 the patient was put on a Lenhartz diet and five days later additions to this diet were made. The temperature, pulse, and respirations continued normal. The stools continued to show blood, mucus, and occasional pus cells. His weight fell to 66.7 kg. During the next two weeks there was no change in the patient's condition except that he was having less epigastric pain and fewer attacks of vomiting. At the end of this period of two weeks diarsenol, intramuscular mercury, and potassium iodide were begun. Four days after the first dose of diarsenol all pain and vomiting ceased. He was put on house diet, and for the first time since admission the stools gave a negative guaiac test, and this was repeatedly negative during this admission. He began to gain weight, and in ten days he had gained 3.5 kg. A total of 1.4 grams of diarsenol intravenously, 1.3 grams of succinimide of mercury intramuscularly, and 20 grams of potassium iodide by mouth was given. He was discharged November 16, 1915, and since then has been under antisyphilitic treatment in the outdoor department. February 18, 1916, three months later, he was still free from symptoms and had gained 10 kg. in weight. A stool specimen showed no mucus, pus, or blood, and gave a negative guaiac test.

In this case the history of a primary sore and the general adenopathy and strongly positive Wassermann reaction in the serum made us certain that the patient had syphilis. The failure to improve under light diet and rest and the remarkable improvement under antisyphilitic treatment indicate that syphilis was the cause of the condition which he presented.

It seems impossible to localize the lesion which caused the symptoms; however, we believe that the bleeding was not of gastric origin, since no blood was noticed in the vomitus until two days before entrance, although he had vomited repeatedly. The blood-stained vomitus was observed only after persistent and continuous vomiting. Following the emptying of his stomach, at which time the

fluid gave a positive guaiac test, he was given a test meal which on removal one hour later gave a negative guaiac test. The stools contained well-preserved red blood cells, pus cells, and mucus. Bismuth roentgen-ray showed no evidence of ulceration in the stomach or the duodenum.

No systematic attempt has been made to review the literature on this subject, but all the standard medical and surgical text-books, including the various systems of medicine, surgery, and syphilis, have been consulted. The opinion is uniformly expressed that syphilis of the stomach is uncommon and that syphilis of the intestine is extremely rare.

DIVERTICULUM OF THE DUODENUM, WITH A REPORT OF A CASE DIAGNOSED DURING LIFE AND SUCCESSFULLY OPERATED ON.[1]

By Seymour Basch, M. D.,

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Diverticulum of the duodenum is a rare condition and one not well known to the profession in general. It has no characteristic clinical symptomatology and, until the most recent advances in radiological diagnosis, its presence was revealed only during a postmortem examination. The writer therefore feels that the following case, diagnosed during life and successfully operated on, is of suffcient interest to be herewith reported.

Case History.—J. L.; female; single; aged thirty-six years; fire insurance agent. Referred by Dr. S. Rosenberg. Patient was first seen by me January 5, 1915, when she gave the following history:

Her family were all rheumatic and very nervous; her mother and one brother died of heart disease. She was left very much to nurses, her dietary neglected, and she remembers that she was a weak, anemic child, very constipated, and often troubled with indigestion. She had had no acute illnesses since childhood, though always thin and pale. Her constipation has persisted despite manifold measures and drugs, and she has often passed large amounts of thick, ropy mucus, with or without feces. In addition, since childhood, she has been troubled more or less with "sour stomach" (heartburn, acid belching, distention, flatulence, etc.), particularly after

[1] Read at the Nineteenth Annual Meeting of the American Gastro-enterological Association, at Washington, D. C.

partaking of sweets, acids, fruits, etc. At times there was even an aching pain in the upper right quadrant, coming on about one hour after meals. These manifestations of gastric indigestion always yielded to strict attention to diet. For years she was troubled with hemorrhoids and rectal fissure, being finally cured, after several previous operations, three years ago by Dr. Kelsey. Six years ago she was operated on for appendicitis at St. Mary's Hospital in

FIG. 1.—Taken prone a few minutes after the bismuth meal. Stomach very active, duodenal cap normal. Note the large round, bismuth-filled pouch between the second portion of the duodenum and the pyloric antrum, apparently communicating with the latter.

Brooklyn. The appendix, she was told, was "large and inflamed, and contained a little pus." Her indigestion, however, was not relieved by any of these operations; on the contrary, it has become progressively worse, and since several months has been particularly distressing despite most careful dieting and medicinal measures. A most annoying symptom has been a sharp, aching pain below the gall-bladder region, occurring one or two hours after meals and lasting for some time.

Status Presens. The patient is very emotional, voluble, and decidedly self-centered; she is thin and pale and appears to be very distressed. The central nervous system is negative, excepting for exaggerated knee-jerks; there are no obvious signs of hyperthyroidism. The pulse is slightly accelerated, soft and regular; blood-pressure is 150 systolic and 95 diastolic. The heart examination reveals a loud aortic stenotic murmur.

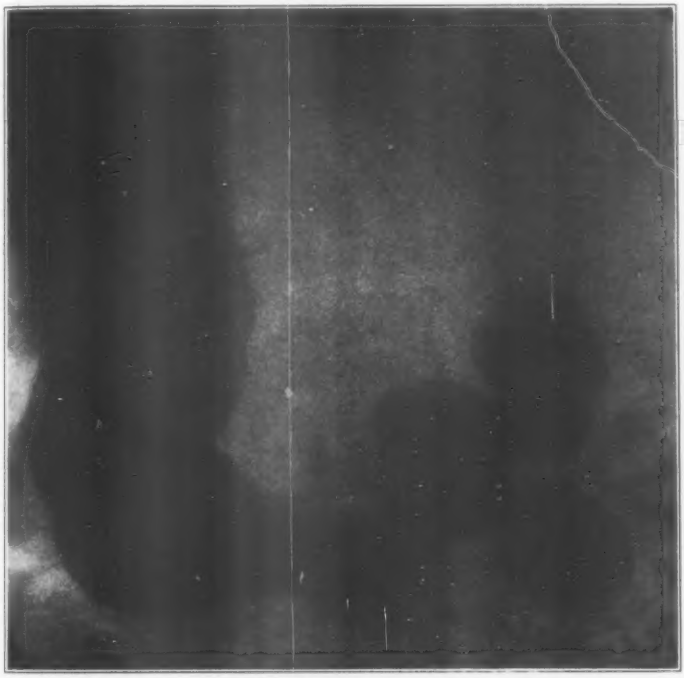

FIG. 2.—Taken erect immediately after Fig. 1. The bismuth-filled pouch occupies the same position, but is seen to be entirely separated from the stomach.

The abdomen is of the enteroptotic type, with a colonic bulge; the right kidney is displaced down to the iliac crest while the left one is ptosed to the second degree. The spleen and liver are not palpable. There is an old firm appendix scar. The gall-bladder region is very tender to pressure, the pain being referred to the right nipple. There is a definite stomach splash, with the greater curvature apparently slightly below the umbilicus.

The feces are soft and bulky, not formed, have a sour odor and strong acid reaction; they show poor starch digestion and are intermixed with a large amount of thick, ropy mucus. Occult

blood is absent and the bile reaction is normal. In the fasting state the stomach is empty, and one hour after Ewald-Boas' breakfast, 2 ounces of contents were aspirated, evidencing no special variation from the normal, and giving 28 free HCl and 60 total acidity.

From the above data the case was regarded as one of chronic inflammatory disease in the gall-bladder-duodenal region, the exact nature of which could not be stated. Chronic duodenal ulcer with possible gall-bladder involvement or adhesions seemed most probable.

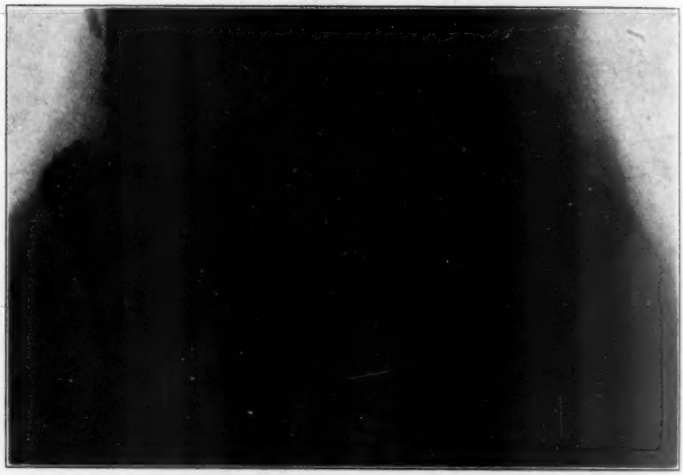

FIG. 3.—Colon enema plate taken ninety-six hours after Fig. 1. There is still a definite though slight amount of bismuth in the duodenal pouch.

January 18, a gastro-intestinal roentgen-ray examination, made by Dr. Arthur S. Unger, gave the following results: The stomach is normal in shape, size, and position; its peristalsis is very active, and it is completely empty within six hours. The bublus duodeni is large and appears overfilled; the cap is normal in contour; part of the first and second portions of the duodenum appear to adhere closely to the liver. Near the commencement of the third portion of the duodenum a distinct bismuth-filled dilatation is seen. It is round and pouch-like in shape and seems to communicate with the duodenum. Serial plates show bismuth retention in this pouch for at least ninety-six hours. In view of these roentgenological findings, the long-standing nature of the case, its resistance to medical therapy, and the recent aggravation of the subjective symptoms, surgical intervention was regarded as the only possible means of relief.

The patient was operated on by Dr. Charles A. Elsberg, January 31. The following was Dr. Elsberg's account of the operation:

An incision of 10 cms. was made through the right rectus. When the peritoneum was opened the pylorus and first and second portions of the duodenum were found to be congested and bound together by numerous fine adhesions. There was no evidence of an ulcer of

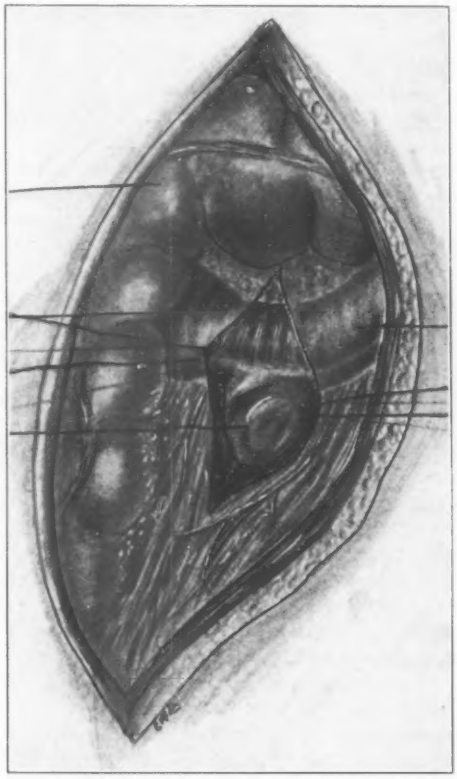

FIG. 4.—Congenital diverticulum of the duodenum at the junction of the second and third portions.

the stomach or the duodenum. The colon was then turned upward the posterior layer of the transverse mesocolon incised, and the third portion of the duodenum exposed. On the lower margin of the duodenum at the angle between the second and third portions was a large diverticulum measuring about 3 x 4 cms., its base about 3 cms. in diameter. The second portion of the duodenum was mark-

edly dilated and hypertrophied, while the third portion was normal in size. The diverticulum was excised at its base in the longitudinal direction, and the opening in the duodenum closed in the transverse direction by a double layer of fine silk sutures. The posterior layer of the mesocolon was then closed by catgut sutures being attached to the suture line and the duodenum. There was no narrowing of the duodenum as a result of the suture. A typical posterior gastro-enterostomy by suture was then performed and the abdomen closed in the usual manner.

The gastro-enterostomy was made because of the periduodenal adhesions and the duodenal dilatation.

The specimen was examined by Dr. E. P. Bernstein, who reported as follows:

Macroscopically the specimen is an intestinal pouch about 3 x 3 x 4 cms., with very thin walls.

Microscopic examination shows the peritoneal coat to be intact and normal; the muscular layer is intact but very thin throughout the entire specimen. The mucous membrane shows numerous defects with loss of the entire mucosa. Where, however, the mucous membrane is present it is normal in character and shows no inflammatory reaction, either acute or chronic.

Diagnosis. We must consider this specimen to be a congenital diverticulum. The loss of mucosa in spots is an artefact.

The patient made a good primary recovery from the operation, and in the short time that has elapsed shows a decided improvement in her digestion. However, in view of the presence of the extensive adhesions, the greatly dilated second portion of the duodenum, the marked enteroptosis, the obstinate constipation, the aortic lesion, and the highly neurotic condition of the patient, anything approaching a complete restoration to health is not to be expected.

This very unusual case is as far as I can learn from an exhaustive study of the literature only the second one to have been diagnosed during life and successfully operated on. The first case reported was one by Forssell and Key[2] in 1915. In their case the location of the diverticulum and the roentgen-ray and operative findings were very similar to those in the one herewith reported. Their patient also had suffered for many years from symptoms of duodenal ulcer. Forssell and Key state that their patient was entirely free from her symptoms after the operation.

It is unnecessary to enter here into any extended discussion of the subject of duodenal diverticulum. Those interested are referred to the writings of Buschi,[3] Bauer,[4] Wilkie[5] and others mentioned in the appended literature. A few remarks intended to

[2] Nord. Med. Arkiv., Stockholm, 1915, Afd. II (Inre Medicin.), Heft. 1, No. 2.
[3] Virchows Arch., 1911, Bd. xxvi, S. 121.
[4] Wien. klin. Wchnschr., 1912, Nr. 23, S. 879.
[5] Edinburgh Med. Jour., September, 1913.

bring out the main points of general interest on the subject may be permitted.

As already stated, duodenal diverticula are of comparatively rare occurrence. There are only between 65 and 70 cases altogether reported in literature. Undoubtedly, the condition is much more frequent than these figures leave one to conclude, for it is easily overlooked unless specially sought for.

According to Buschi, from whose comprehensive study, in 1911, the following facts have mainly been gathered, Chomel,[6] in 1707, reported the finding of a duodenal pocket containing 22 stones at an autopsy on a woman, aged eighty years. This patient, Chomel stated, had always felt a pain at the site of the sac about two hours after meals. Morgagni,[7] in 1839, however, gave the first real description of a duodenal diverticulum.

Duodenal diverticula have been found twice as often in the bodies of males as in those of females, about 80 per cent. of them in individuals over fifty years of age. Over 75 per cent. of the diverticula were located in the second portion of the duodenum, and more especially in the region of the papilla of Vater, and of the opening of the duct of Santorini; hence, the French designation of "diverticules perivateriens." Of 44 cases tabulated by Buschi, the second portion of the duodenum was involved 33 times, the first 6, the third 3, and first and second in the same individual twice. In most instances only one diverticulum has been found in a case, although as many as five have been reported. Thus, Buschi found 35 cases with a single diverticulum, 13 with two, 2 with four, and 2 with five diverticula. The shape varied, being usually spherical or hemispherical; it may, however, be ovoid or like a gloved finger.

In size these pouches range from a few millimeters to 5 cms. in their greatest diameter. The opening may be narrower, but usually is fully as wide or even wider than the cavity of the sac. In a few instances a valve-like fold has been seen at the opening. The width of the opening and the shallowness of the pouch prevent the disastrous consequences so common in Meckel's diverticulum and the vermiform appendix.

The sac has generally been found empty and flaccid; at times, however, it has contained fluid or food remnants, or even stones.

Most investigators report the sac wall as being composed entirely of mucous membrane and submucosa, the mucous membrane being smooth, thin and free, or almost free, from glands. The muscular layer is said to be absent or to appear only as a ring about the opening of the pouch. Buschi, Voelker,[8] Seipel[9] and others,

[6] Histoire de l'Acad. royale, Paris, 1710.

[7] De sedibus et causis morborum, etc., Firenze, 1839.

[8] Beiträg zur Kenntnis d. falschen Darmdivertikeln, Inaug. Dissert., Freiburg, 1906.

[9] Ueber erworbene Darmdivertikel, Inaug. Dissert., Zürich, 1895.

however, found perfectly normal mucosa and some muscle bundles which extended far into the sac, in some instances even to the distal end, being then very atrophic. In our own case the pathologist reports that "the muscular layer is intact, but very thin throughout the specimen."

Diverticula occur only exceptionally on the outer or anterior surfaces of the duodenum; in most instances they are on the inner aspect in contact with the head of the pancreas, from which they are separated by loose connective tissue. Frequently they indent the head of the pancreas, or are intimately connected with the common bile duct or the duct of Wirsung, which usually lie behind the diverticula.

The question of the origin of these diverticula has given rise to much discussion and to a number of interesting theories. Those interested in the details are referred to the papers of Buschi, Wilkie, and Davis,[10] in which the question is gone into at length. Buschi himself concludes that they are to be regarded as of congenital origin, and gives detailed reasons for his conclusions. He states, however, that the possible occurrence of false or acquired diverticula through stones, tumors, ulcers, and similar causes cannot be disputed.

Until the publication of Bauer's two cases in 1912 no serious clinical or pathological significance was attached to duodenal diverticula. In Bauer's first case there had been signs of pyloric obstruction, and, despite a posterior gastro-enterostomy, the patient died ten days after the operation. The autopsy showed two duodenal diverticula, the larger one of which was about the size of a hen's egg, and situated on the inner pancreatic aspect, involving both the common bile and Wirsung's ducts. Bauer believed that this sac through tension when full caused an insufficiency of the pylorus and a stenosis of the duodenum. In Bauer's second case the duodenal diverticulum was an accidental postmortem discovery. It was filled with a feculent mass, and the duodenum itself was much inflamed and coated with tough, tenacious mucus; the papilla of Vater was inflamed and swollen and closed by a mucous plug. The common bile duct was dilated and the gall-bladder widely distended and filled with stagnant bile. Bauer concluded that in all probability the diverticulum through its feculent contents was the cause of the imflammatory changes in the duodenum and in the bile passages. In two of Wilkie's cases the diverticula were associated with grave disturbances in the adjacent organs, viz., duodenitis and biliary stasis in both cases, while in the first case, there was also an hepatic cirrhosis and in the other an acute hemorrhagic pancreatitis. Wilkie is unwilling, however, to say with certainty that the diverticula were responsible for all the biliary and pancreatic troubles, but thinks there is strong presumptive evidence of an etiological relationship.

[10] Tr. Chicago Pathol. Soc., February, 1913.

In addition to these 4 cases of definite secondary or associated pathological changes reported by others, the radiographic studies of Forssell and Key's case and of my own have unquestionably demonstrated that food and other solid duodenal contents can and at times do enter into these pouches, and remaining there at least four days must undergo fermentation or stagnation, giving rise to very unpleasant local and even far-reaching secondary effects. The marked distention of the second portion of the duodenum and the hypertrophy of its walls in my own case were undoubtedly due to efforts on the part of the gut to force out the contents of the diverticulum. Many of these cases, like Forssell and Key's and the one herewith reported, undoubtedly go on for years with symptoms very suggestive of duodenal ulcer. Now, these cases cannot be diagnosed clinically unless they have real pouch formations which present unmistakable roentgen-ray pictures; frequently, they are so located that ordinary exploratory laparotomy does not reveal them and even at autopsy they may be overlooked unless specially sought for. Is it not therefore possible that a case of clinically suspected duodenal ulcer, reported as not present by the surgeon after operation, may after all at times have been one of these diverticula or even a real ulcer situated not in the usual site, viz., the first portion of the duodenum, but in the second or third portion?

CONCLUSIONS. 1. Duodenal diverticula are of more frequent occurrence than would appear from the number of reported cases.

2. Unless specially sought for they are easily overlooked at operation or autopsy.

3. They can be diagnosed by roentgen-ray examination when they form distinct pouches.

4. They may produce symptoms sufficient to require surgical interference.

5. They can be cured by operation.

THE USE OF RAW EGGS IN PRACTICAL DIETETICS.

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DURING the past fifteen years evidence has been gradually accumulating which shows that raw egg-white occupies an exceptional position among native protein foodstuffs. Pawlow (1902) observed that this substance has only a feeble ability to stimulate a flow of gastric juice. It acted in this way only as so much water.

Cooked egg-white, on the contrary, calls forth an abundance of juice and unites easily with the hydrochloric acid. On account of the scanty supply of secretion which it induces the raw protein has little opportunity to be digested, but this slender chance is still further diminished by another unusual property. Beaumont (1833), during his famous experiments on Alexis St. Martin, was the first to note that native egg-white left the stomach very rapidly in comparison to other foods, including cooked egg-white itself. Indeed, this substance spent a shorter time in the stomach than any other Beaumont investigated. This observation has more recently been confirmed by Cannon (1904) and by London and Sulima (1905). The former found that the egg-white passed through the pylorus at a rate comparable to that of the carbohydrates, which are among the first foodstuffs to enter the intestine after ingestion. Proteins leave the stomach slowly and egg-white was the only exception noted among those investigated. London and Sulima found that this hasty exit from the stomach was most striking. A few moments after ingestion the egg-white escaped in large gushes through a pyloric fistula. During its stay in the stomach it retains its alkaline reaction and passes into the intestine, for the most part entirely unchanged. After feeding a dog native egg-white these workers recovered large amounts unchanged from a fistula as far down the canal as the ileum.

But even this does not exhaust the means by which raw egg-white escapes gastric digestion, for Abderhalden and Pettibone (1912) and Bizarro (1913) discovered that it offers considerable resistance to the action of pepsin. If, however, the egg-white is coagulated it is more readily acted upon by the pepsin, and proteolysis proceeds further.

We may picture this native protein then as quickly leaving the stomach, accompanied by scanty amounts of gastric juice and little altered by pepsin. This peculiar behavior is consistently carried on in the intestine. Bruno and Klodnizki (1914) and Okada (1915) showed that little or no bile was passed into the intestine after the ingestion of raw egg-white, whereas the same material cooked always caused a good flow of bile.

Once in the intestine the native egg-white continues to oppose the digestive enzymes, for it has remarkably strong antitryptic properties. The trouble is not that trypsin is unable to act upon the protein but that the rate of action is so slow. Bayliss (1908) found that it required seventy hours for the digestion of the raw material to equal that of the cooked, all other conditions being the same in the two cases. Indeed, the trypsin appears not to change the egg-white at all. Vernon (1904) found the antitryptic action to be more marked with this protein than with any other. Hedin (1907), Cohnheim (1912), Abderhalden and Pettibone (1912), Long and Johnson (1913), and Bizarro (1913) have all demonstrated

the strong antitryptic action of egg-white. Not only does it resist digestion itself, but it prevents the digestion of other easily digested proteins, as observed by Delezenne and Pozerski (1903), Vernon (1904), Compel and Henri (1905), and Hedin (1907). This suggests that the true cause of both facts is that the colloidal egg-white absorbs the trypsin, thus cutting down its activity in much the same way as the charcoal in the experiments of Hedin (1906 *b*). Recently it has been shown by Maxwell (1915) that boiled starch absorbs pepsin and so hinders its activity.

In view of both its antipeptic and antitryptic action it is interesting to note that other proteolytic enzymes are also unable to successfully cope with this native protein. Chittenden, Joslin and Meara (1892), and Chittenden (1894) showed that raw egg-white was much more poorly digested than coagulated egg-white by bromelin, the proteolytic enzyme present in the pineapple. Jonescu (1907) and Sachs (1907) found that papain was also practically unable to act upon native egg-white.

Preliminary heating of the egg-white greatly increases its digestibility by trypsin. Talarico (1910) found that there was no effect, however, until the temperature reached 70°, after which there was an orderly liberation of amino-acids up to 130°. Frank (1911) also found cooked egg-white to be better digested than raw, the optimum temperature in his experience being 70° to 75°. Bizarro (1913) considered the best temperature for this preliminary heating to be 80°. Abderhalden and Pettibone (1912) and Long and Johnson (1913) made similar observations.

This brief review of its properties shows that native egg-white offers such obstacles to digestion as to place it in an exceptional position among the proteins. This raises the question as to how the body handles such a substance. Very little upon this point has, up to the present, been recorded, although raw eggs and egg-white have enjoyed a great vogue as the mainstay of various diets, especially for the sick. Steinitz (1898) noted incidentally that raw egg-white caused vomiting and diarrhea in dogs, but this interesting observation remained unnoticed. When the same facts were observed again by Mendel and Lewis (1913) they led to an extended study by the author, carried out during the past year, the details of which have been published elsewhere. This showed native egg-white to be a decidedly indigestible substance. When fed to dogs in any considerable quantity it invariably caused diarrhea and sometimes induced vomiting. The severity of the diarrhea depended largely upon the amount of material ingested, but also, to a less extent, upon the individual susceptibility of the subject. With dogs of 5.5 to 7 kilos in weight four or five egg-whites were sufficient to cause more or less severe diarrhea. Even the whites of two eggs often caused softening of the feces. The stools were abnormal in character, very offensive

in odor, and often contained much mucus. After the ingestion of even small amounts of native egg-white the latter could be recovered unchanged in small quantity from the stools, and when the amount ingested was large the proportion of coagulable protein in the feces was correspondingly increased.

Even when the feces appeared normal undigested egg-white could usually be recovered. In this connection, Tsuchiya's (1908) statement that albumin is never found in normal feces is pertinent.

After eating enough egg-white to give rise to diarrhea the dogs usually lost weight. In a few cases small intestinal hemorrhages were observed. Occasionally samples of urine obtained by catheterization were found to contain small amounts of protein. In all these reactions there was found much variation in the sensitiveness of the subjects, for sometimes a large dog was more easily affected than a small one by the same amount of protein.

It made little difference with the action of the egg-white whether it was eaten alone or mixed with other food. In the latter case the diarrhea was later in appearing. The presence in the food of a substance able to cause a good flow of gastric juice—meat extract for example—had no effect upon the time of appearance or severity of the diarrhea.

It was soon noticed that when the raw protein was fed for several days in succession its ill effects gradually waned. The time necessary for the abatement of the diarrheal action varied from three to five days. If now the ingestion were continued there ensued a period of alternate days of diarrhea and constipation, after which the egg-white ceased to exert any marked action. The tolerance thus developed lasted for a short time even after the feeding of the uncooked material was discontinued. This recalls the tolerance acquired by dogs who receive peritoneal injections of raw egg-white. Cramer (1908), Hamburger (1908), and Oppenheimer (1904) have observed that under such conditions the dogs utilized part of the protein and excreted the rest in the urine. After repeated injections the quantity used rose gradually. It might be supposed that all proteins would appear, at least in part, in the urine after injection intraperitoneally, but Mendel and Lockwood (1904) have shown this not to be the case with edestin and excelsin.

Native egg-white was found poorly utilized. In large doses from 30 to 50 per cent. of that ingested was wasted by being ejected with the feces. After the dogs had grown to tolerate this material it was better utilized, but even in these cases the best figure was about 85 per cent. When Mendel and Lewis (1913) fed this substance to dogs only about half of the nitrogen in the meals appeared in the urine for the following twenty-four hours as contrasted with almost all when meat, casein, and other proteins were fed instead of the egg-white. Steinitz (1898) reported

unchanged egg-white in the feces in considerable quantities. Vogt (1906) and Falta (1906) found that the nitrogen in uncooked egg-white superimposed upon a standard diet was excreted in the urine much more slowly than that ingested in the form of other proteins.

Drying the egg-white at low temperatures did not abate its diarrheal activity nor improve its utilization. Neither did long standing. Falta (1906) also made experiments, using desiccated material, and found in three cases a utilization of 80 per cent., 80 per cent., and 61 per cent. respectively. LeClerc and Cook (1906) found the same substance very poorly utilized.

When dogs ate cooked egg-white in place of the native or desiccated protein they did not have diarrhea and the material was excellently utilized, the utilization being in the neighborhood of 90 per cent. When raw and cooked egg-white were fed on alternate days or periods the differences in the utilization and in the nitrogen balance were striking.

Experiments were made to show at what temperature the change in digestibility became effective. By heating for thirty to forty-five minutes in a double boiler with constant stirring the egg-white suffered little impairment of its activity in causing diarrhea up to 55°. Above this the activity is considerably decreased and disappears entirely at 70°. It should be noted that above 55° coagulation begins and at 70° the protein is entirely coagulated, but is very soft and jelly-like in texture.

In order to show that dogs did not have an exceptional inability to digest native egg-white, experiments similar to the above were made, using rats and rabbits as subjects. These had in both cases the same results. Both rats and rabbits had diarrhea with consequent poor utilization of the protein. The hardy rats, however, were less sensitive than the other animals. That this native protein sustains life in rats poorly in comparison to others is the general conclusion drawn from the work of Falta and Noeggerath (1906), Knapp (1908), Maignon (1912), and Frank and Schittenhelm (1912). Von Knieriem (1885) and Röhmann (1914) reached the same decision from work with mice as subjects. Osborne and Mendel (1911), on the contrary, kept rats growing well on rations containing cooked egg-white as sole protein for as long as one hundred and seventy days. Von Knieriem (1885) found that desiccated egg-white caused rabbits to pass very soft and abnormal feces containing much unchanged egg-white. Mendel and Rose (1911) found it impossible to feed any large quantity of raw egg-white to rabbits without inducing diarrhea.

No other native proteins are known to act in the alimentary tract in the manner brought out by these experiments. On account of the importance of the subject from the stand-point of dietetics it was of interest to determine how raw egg-white

comported itself when ingested by man. The experiments described below lead to the same conclusions already formulated.

The first group of subjects included a number of men and women partaking of a diet consisting largely of raw eggs and milk for the purpose of increasing weight.

CASE I.—Subject O. B. This was a man, aged twenty-five years, who took two to three raw eggs beaten up in milk three times a day. During the first three days there was rather severe diarrhea and general malaise and after that regular stools of soft consistency. The subject had previously been somewhat constipated.

CASE II.—Subject D. S. was a man, aged forty years, who also took two raw eggs beaten up in milk three times a day. He did not experience diarrhea, but did have regular stools sometimes twice a day, whereas before beginning the diet he had had somewhat obstinate constipation. He drank a large quantity of milk which generally would tend to prevent diarrhea.

CASE III.—Subject M. R., a woman, aged twenty-five years, ate six to eight raw eggs per day. The first few days there was extensive diarrhea followed for some time by irregular movements, consisting usually of soft material.

CASE IV.—Subject M. H., a young woman, aged twenty-two years, who ate two raw eggs at night and the same number in the morning. There was no decided diarrhea, but previous constipation was overcome and the stools were soft. This subject complained of some intestinal discomfort.

CASE V.—Subject D. G., a woman, aged thirty-five years, took two or three raw eggs in milk three times a day. In this case there was diarrhea for two days, although not severe. This was followed by a day without a stool, after which the bowels moved regularly every day. There had been no previous constipation.

CASE VI.—A man, aged about thirty-five years, took each night before retiring two raw eggs in whisky. On almost every such occasion he suffered much intestinal discomfort, accompanied with colic-like pains. Considering raw eggs to be "bland" and the whisky beneficial he did not discontinue the treatment for some time.

Another group of subjects ate only the whites of raw eggs experimentally.

CASE I.—Subject D. S., a young woman, aged eighteen years, was unaffected by eating the whites of two eggs per day. When the number was doubled, diarrhea ensued accompanied by discomfort and some trouble with intestinal gases.

CASE II.—Subject B. B., aged thirty years, remained unaffected by eating every morning the whites of two to four eggs. She did notice discomfort and accumulation of gas. When the number was increased to six per day the subject complained of malaise and took an aversion to the diet. There was flatulence but no diarrhea.

CASE III.—Subject A. B., a child, aged three years. One-half of a raw egg-white ingested each day led to such laxness that the experiment was discontinued after the third day. The diarrhea, then, disappeared at once.

CASE IV.—Subject J. B., aged five years, was, on the contrary, quite unaffected by the same amount of egg-white as was given the last subject.

CASE V.—Subject W. B., a man, aged thirty years, was found quite unsusceptible to the native egg-white, since two to six whites failed to cause any noticeable change in the feces. When half a dozen eggs were eaten at once he experienced decided discomfort, associated with flatulence. An analysis of the stool for nitrogen showed the protein ingested to be only 85 per cent. utilized. Even eight to nine raw whites eaten at one time did no more than soften the feces, but the utilization was still poorer than before, being only 77 per cent. At no time was there any protein in the urine.

CASE VI.—Subject L. M., aged twenty-five years, ate the whites of six raw eggs every third day. On each occasion the stool was soft and unformed.

Falta (1906) found this material to be utilized by man to the extent of 70 per cent. Wolf (1912) reported a still lower value, namely, 50 per cent. In the latter case the feces were of soft consistency although no diarrhea was observed. There was over twice as much nitrogen in the feces when the raw egg was in the diet as when the food contained the same amount of nitrogen in the form of other proteins. On one day there was more nitrogen in the feces than in the urine. The latter did not contain albumin.

Hamburger (1902) and Cramer (1908) claim that albuminuria follows the ingestion of large doses of native egg-white by man. Oertel (1883) had not been able to find albumin in the urine of either dogs or men after the ingestion of large quantities or raw or half-cooked egg-white. Neither did this material cause an increase in excreted albumin in preëxisting albuminuria. Another aspect of this debated problem will be considered later.

It is a matter of common experience that cooked egg-white has not been known to cause any exceptional digestive effects, and is well utilized. Rubner (1879), who seems to be the sole investigator to have fed a subject on cooked eggs only, found the utilization to be 97 per cent. Cathcart and Green (1913) found a delay in the excretion of nitrogen after superimposition of both native and coagulated egg-white, but the delay appears greater in the sulphur than in the nitrogen elimination. These authors and Wolf (1912), who noticed the same facts, believe that the sulphur complexes in the uncoagulated egg-white have power to withstand the digestive enzymes.

Raw egg-white can be made digestible by other means than

heating at 70°. This result can be brought about by incubation with dilute acids and alkalies at 37°; by precipitation with alcohol, chloroform, or ether; by partial digestion with pepsin, and by conversion into alkali metaprotein.

Egg-white is not a homogeneous substance, but consists of at least four components—ovoglobulin, ovalbumin, conalbumin, and ovomucoid. These were separated according to the method of Osborne and Campbell (1900). When fed to dogs the albumin fraction proved to be the indigestible constituent, a result in harmony with the observations of Mendel and Lewis, who found that purified ovalbumin caused profuse diarrhea when fed to dogs. Vernon (1904) states that crystallized albumin is even more resistant to trypsin than native egg-white.

All the experiments so far described were made with egg-white from the egg of the common fowl. That it is not unique in its unusual behavior in the alimentary tract was shown when the egg-white from the egg of the duck was found to act in exactly the same manner.

In contrast to egg-white, egg-yolk was found to be well digested and utilized. There appears to be nothing in the literature to suggest that the latter is indigestible. Mendel and Lewis's (1913) experiments showed the excretion of nitrogen after feeding ovovitellin to be the same as that after meat, a result in opposition to that obtained with both coagulated and uncooked egg-white. In the author's experiments the feeding of egg-yolk either cooked or raw in any quantity of dogs usually caused a rather severe digestive disturbance, of which vomiting was the main symptom. The vomitus contained much bile and sometimes this liquid was alone expelled from the stomach. This suggested that the high fat content of the yolk was the cause of the trouble. This assumption was correct, for when the fat was extracted the residue of crude ovovitellin was eaten by dogs with no untoward effects.

These experiments show, then, that raw egg-white is a decidedly indigestible substance. It may cause diarrhea and vomiting when ingested in any large quantity. Its utilization by the body is poor, since it is used only to the extent of from 50 to 70 per cent. What bearing have these facts upon practical dietetics?

It is difficult to say to what extent raw eggs are ordinarily used. Since there is a wide-spread idea that they are especially digestible and very nutritious, one might expect their use to be common. There is no doubt that this is so when the diet in disease is considered, for raw eggs appear to play an important part in systems of dietetics for the sick. It is likely that Beaumont's (1833) observations gave the first impetus to this dieto-therapeutic movement. According to his views digestion takes place in the stomach and absorption in the intestines. The criterion of digestibility was the time a food remained in the stomach, the assumption

being that it passed the pylorus only when properly prepared by digestion for ensuing absorption through the intestinal mucosa. Since native egg-white left the stomach more rapidly than any other food the conclusion seemed obvious that it is a very readily digested substance. Beaumont says:

"Albumin if taken into the stomach either very slightly or not at all coagulated is perhaps as readily chymified as any article of diet we possess. If coagulated it experiences a very protracted digestion. In the first case the albumin becomes finely coagulated and divided in the stomach."

While the fact that raw egg-white does remain in the stomach only a short time is true, the interpretation of the fact was erroneous. These experiments of Beaumont, the first of their kind, attracted much attention and became widely known. The earlier writers on dietetics based their advice in many details upon his work. Chambers in his *Manual of Diet* (1875), after quoting a table of Beaumont's showing the times spent in the stomach by raw eggs and eggs cooked in various ways, says,

"It may be observed that this is just the order in which they are tasty—that is to say, the degree in which they come with facility into contact with the sensory nerves distributed through the mucous membrane—so that duty and pleasure here, as usually in natural operations, become one."

To such a school nature is always right; it would not be thought possible for her to be so mistaken as to allow albumin to leave the stomach practically undigested.

Although these early views on digestion are no longer supported by such arguments they still appear to be accepted almost unquestioned. In 1906 a Farmers' Bulletin of the United States Department of Agriculture quotes Beaumont's work and helps to spread the impression that raw eggs are very easily digested, since they are "chymified" in one and a half to two hours as against three for soft-boiled eggs. The figures for "artificial digestion," which approximated bodily conditions as closely as possible, are even more impressive, since it appears that it requires eight hours for the digestion of hard-boiled eggs, six hours for soft-boiled eggs, and only four hours for raw eggs. This bulletin, which has been extensively circulated, gives also the results of experiments which show that cooked eggs are thoroughly digested. Still more recently in *Practical Dietetics for Nurses*, Pattee (1910) quotes, "Half subtilized to chyme the liquid food readiest obeys the assimilating powers." Egg-white is then listed as a liquid food and the proper conclusion thus drawn. This notion of the easy assimilation of liquid foods is often mentioned by writers on dietary topics in their discussion of egg-white, and it is taken for granted that such a substance offers little resistance to the digestive juices. How far astray such an assumption may lead one has already been shown.

In the larger and more recent text-books on dietetics the use of raw eggs is generally recommended. Thompson, whose book *Practical Dietetics* is widely used and much quoted, says on this topic:

"Whole raw eggs are very popular in dietetics at present and are often prescribed when a nutritious, highly concentrated food is desired, as in cases of tuberculosis, some forms of anemia, and various wasting diseases; sometimes from eight to ten or twelve are given daily if they can be digested."

Egg albumen is said to be well absorbed and many recipes are given for preparing albumen water in a palatable form. It is stated, without naming Beaumont, that "a raw egg is ordinarily digested in the stomach in one and a half hours, but a baked egg requires from three to four hours."

In *Diet in Health and Disease*, by Friedenwald and Ruhräh (1913), raw eggs are still more strongly recommended. These authors state:

"In various diseases accompanied by loss of flesh and strength, raw eggs in large numbers are prescribed, as many as twenty-four eggs being given in twenty-four hours. Egg albumen is best absorbed when eaten raw. Eggs beaten up in milk are very useful for the diet of the aged when there are diminished powers of digestion. Raw eggs sometimes disagree but this is more often due to faulty preparation than to any real egg idiocyncrasy. In tuberculosis raw eggs are of the greatest value; six to twenty-four whites may be given daily."

These writers—Thompson, Friedenwald and Ruhräh, Pattee, Winthrop (1899) and others—advise raw eggs as part of the diet in the treatment of many diseases, such as typhoid, diphtheria, gastric ulcer, tuberculosis, appendicitis, gastritis, chronic indigestion, etc. We read that "In fevers albumen water helps to supply wasted tissue albumin;" that "Raw eggs in consumption are full of nutrition and very assimilable;" that "Albumen water is utilized by infants, being found very useful in disorders in which some nutritious and easily assimilated food is needed." It is more surprising to find raw egg-white apparently advised in diarrhea and contra-indicated in constipation; to find raw eggs and albumen water prescribed in dysentery, in chronic cases of which "egg albumen and beef juice form the main part of the diet." Again, it is often stated that raw egg-white can be retained or "kept on the stomach" when nothing else can. This is not really true, since it leaves the stomach rapidly, but in a sense contrary to that meant!

In the treatment of typhoid most writers are agreed that indigestible food should not be fed and that "those causing the least intestinal debris" are the best; yet they all unite in advising raw egg-white in the diet. In the current therapy of gastric ulcer albumen water is frequently used, with the object of taking up the

excessive acid. Insofar as it calls forth no more gastric secretion its use may be beneficial, but considering the speed with which it escapes through the pylorus its efficiency in removing acid already present is problematical. One writer says: "The egg-albumen should be prepared in such a manner as to require the least possible expenditure of force in digestion." Cannon (1904) has shown that the intestine expends more motor activity upon the absorption of the carbohydrates than upon that of the fats or proteins. Raw egg-white, however, acts like a carbohydrate in this respect. Another author states that native egg-white is especially valuable for those with a "weak digestion." All the evidence gathered in this paper tends to show that the substance in question requires an exceptionally "strong digestion" if it is to be utilized.

The most whole-hearted advocate of raw eggs appears to be Dr. Ely (1903), who, in "The Fable of the Egg," shows himself a bold practitioner of his own ideas. Again, Beaumont is quoted with nothing to show that anything has been added to the subject in the eighty years since his observations. The number of eggs advised and administered may seem "fabulous," as the author admits. One patient ate 3006 raw eggs in a year while another partook of 5475 in the same time, the latter being "an exemplary subject as to eggs." It is further stated:

"Some moral force is necessary on the part of patient, nurse, and doctor to overcome a repugnance to the treatment. It is to be understood that in every instance they [eggs] have been used for their supporting and restorative influence. Although some patients have died while taking eggs I can think of no case in which death was due to their liberal use. If you give eggs to your patients do not be chicken-hearted in their employment. Do not fear the production of albuminuria from the ingestion of a large amount of egg albumen. Notwithstanding all possible efforts, nausea and vomiting and diarrhea may often be produced and the physician may be thwarted in his object. He will then try the whites of eggs alone. I have given the whites of forty-eight eggs daily for many days to a patient in the critical stages of typhoid fever. Please remember that I am not advocating a fad, specific, or 'cure-all.' I would urge that in some chronic cases of exhausted nerve centers, and in those acute, critical cases that tax resources for maintaining life, they [doctors] should throw away their tonics and possibly stimulants and should gradually lead the stomachs of their patients up to the egg-an-hour practice."

Enough has been quoted, perhaps, to show the reasons hitherto underlying the advocacy of raw eggs. The results of the present study show these reasons to be not well supported and indicate that the use of raw egg-white is decidedly inadvisable. A substance which fails to stimulate a flow of gastric juice and is antipeptic, which hurries from the stomach, calls forth no flow of bile,

and strongly resists the action of trypsin, which is poorly utilized and may cause diarrhea, has evidently little to recommend it as a foodstuff of preference for the sound person, let alone for the invalid. And when the native protein needs only to be coagulated at 70° in order to obviate almost all the effects mentioned, there appears still less reason for using it uncooked. Other considerations strongly support this conclusion. For instance, Stokvis (1864) declared that raw egg-white eaten in quantity is absorbed undigested and excreted in the urine, doing thereby some damage to the renal epithelium. For a number of years this work was disputed by some and confirmed by others. Ascoli (1902) clarified the situation somewhat by stating that the alimentary albuminuria is not generally manifested by sound persons but usually is by the sick. Besides his own observations he cites other investigators who found that small kidney lesions were caused in this way. The amounts of egg used by Ascoli were not unduly large. The work of Hamburger, Oppenheimer, and Oertel on this topic has already been mentioned. It should be stated that the subject is still a debatable one.

It is true that fairly large amounts of raw egg-white need to be ingested for the abnormal digestive effects to be made manifest; but even if small quantities are used, certain disadvantages may follow. The indigestible protein may reach the large intestine and there become a good pabulum for the putrefactive bacteria. Or mixed with other foods it may retard the digestion and lower the utilization of other proteins. Again, it seems more than a coincidence that of all the common proteins egg-white is the most indigestible and at the same time the most common cause of anaphylaxis. According to the latest views on this subject, as stated by Wells (1914), anaphylactic intoxication is caused by the entrance into the blood of intact, foreign protein molecules. If this be so, it would appear that egg-white is a substance peculiarly apt to be the agent in allergy. It leaves the stomach practically unchanged, so that in the intestine it may be absorbed still intact or only slightly altered. The strong antitryptic action it possesses leads to the same danger. Lately, Van Alstyne (1913) has shown that egg-albumen can enter into the circulation unaltered and is excreted in the urine. In order to cause anaphylaxis it appears unnecessary that large amounts should enter the blood, for Wells (1914) has shown that in guinea-pigs sensitivity has been produced with one twenty-millionth of a gram (0.00000005 gm.) of crystallized ovalbumin and fatal results are obtained after sensitization with one millionth of a gram (0.000001 gm.). In fact, small amounts are frequently more effective than large. It may be argued that cleavage products of any protein may be absorbed in small amount. This is true; but Wells has found that the protein molecule loses its anaphylactic properties as soon as it is altered to any extent.

He was not able to get reactions from the proteoses of egg-albumen. Ten Broeck (1914) found that racemized egg-white had no anaphylactic effect either toward itself or toward native egg-albumen. The simpler the protein disintegration products become the less toxic is their action. The thorough gastric proteolysis undergone by practically all proteins except raw egg-white is a potent factor in preventing allergy. It is well established, however, that even cooked egg-white cannot be used by those sensitized. This does not weaken the case against raw egg, for, as already stated, the coagulated egg-white leaves the stomach little less rapidly than the uncooked. In the texts and manuals on dietetics quoted above the advice to use raw or even cooked eggs is frequently safeguarded by the caution that certain people are peculiarly susceptible to this foodstuff, and it would appear from the cases cited in professional journals that such sensitiveness is not uncommon. Schloss (1913) reported an interesting case in which the feeding of raw egg-white to a child ten days old caused it to react for years to either cooked or uncooked egg-albumen. The sensitizing substance appeared to be ovomucoid while ovalbumin seemed to be inactive.

With the improved technic for rectal feeding effected by the drip method there has come an increased interest in this kind of alimentation. Since the foods used must be liquid it is natural that raw egg-white should suggest itself for the protein requirements. As early as 1869, Voit and Bauer, however, concluded that this foodstuff was practically worthless for the purposes, a conclusion also reached by Eichorst. Previously it had been stated that salt aided in the absorption of the egg-white, but Eichorst doubted this and stated that the salt caused diarrhea. Czerny and Latschenberger (1874) and Ewald (1887) also found the salt to be of no value. More recent studies of rectal alimentation tend to show that the amount of protein which can be utilized in this way is unimportant compared to the requirements of the body, a conclusion supported by the work of Adler (1915). Furthermore, it is considered doubtful if unaltered proteins can be absorbed from the colon (Pfeiffer, 1906). If this is so, native egg-white must be considered an especially poor substance for nutrient enemas in view of its pronounced antitryptic properties.

It must not be assumed from the foregoing discussion that native egg-white is considered a toxic or otherwise dangerous substance. But the evidence regarding its behavior in the alimentary canal is taken to show that no advantage accrues to the body by using it raw rather than cooked. Furthermore, when the diet of those seriously ill is considered it may fairly be asked in the light of scientific evidence if the current extensive use of raw eggs is not illogical and inadvisable?

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THE TREATMENT OF BRONCHIAL ASTHMA BY VACCINATION, WITH REPORT OF CASES.

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UNTIL recently Osler has described asthma as "so imperfectly understood that it is impossible to give a satisfactory definition." The pathology included spasm of the bronchi and spasm of the respiratory muscles and diaphragm and vasomotor disturbances of the bronchial mucous membrane. Etiology included heredity, a neurotic basis, and in addition other factors, such as nasal obstruction by polypi and hypertrophied turbinates, climatic effects, and gout.

Measures for cure generally proved useless; to help the individual attacks, adrenalin, morphin, strychnin, atropin, potassium iodide, lobelia, stramonium, and asthma powders have all been extensively used, but no means of preventing future attacks has been found.

Although we must admit that asthma is still imperfectly understood and that its etiology is not always clear, yet the past few years have added much information which will without doubt be a clue to the eventual relief of this harassing malady.

When a foreign proteid is injected in minute quantities into the animal body, sensitization occurs; the injection of a large amount of the same proteid[1] after a certain interval of time (usually twenty-one days) results in a set of symptoms characterized by sneezing, labored breathing, skin eruptions, joint and glandular swellings, edema, and cardiac palpitation; if the attack be severe enough, convulsions and death follow; this reaction is called anaphylaxis. Anaphylaxis implies a hypersensibility; either a natural one exemplified by an attack of hay fever or serum sickness, or an artificial one brought about for example by a previous injection of horse serum.

Animal experimentation[2] has taught us that when the foreign proteid is injected into the body in proper amounts, specific antibodies or amboceptors are produced for this proteid; if after certain periods of time the injections be repeated in constantly increasing quantities, some of these antibodies in the presence of compliment and antigen, are protective; this holds true whether the invading substance be introduced subcutaneously, intravenously, intraperitoneally or by mouth. The foreign proteid contains two sub-

[1] Rosenau and Anderson: Hygienic Laboratories Bulletin, 1908, Nos. 29 and 45.
[2] Zinsser, H.: Anaphylactic Phenomena. Harvey Lectures, 1914–1915, series No. 10.

stances, one toxic which may cause death, and one which immunizes the individual.[3]

Immunization is obtained by introducing this foreign proteid into the system in small quantities frequently repeated and in increasing doses, within seven or eight days each, during the pre-anaphylactic or anti-anaphylactic period; if the period be too long the hypersensitive state may lead to serious or fatal consequences; this hypersensitive state may be transmitted from mother to offspring.

Bacterial anaphylaxis is not so readily produced as that by foreign albumens, as egg and serum albumens.

Food protein is absorbed as amino-acids and then reconverted into protein in the proper form for utilization; if by any chance it undergoes incomplete breaking down, and some of the by-products are absorbed, sensitization occurs; if after a certain time (ten to fourteen days) the same article is again eaten, anaphylaxis results in the form of asthma, urticaria, or erythema (the so-called indigestion rash). This same sequence probably occurs in the case of injected proteids, whether horse serum, bacteria, or pollen; if not converted into a proper and available form for use, their by-products sensitize the individual so that a second dose is anaphylactic.

Asthma is undoubtedly in some cases an expression of anaphylaxis; clinically it resembles the hypersusceptibility produced in animals by the injection of foreign proteid. Patients with this disease become sensitized to some form of proteid by absorption from the nasal mucus membrane, alimentary canal, or from some focus of infection, and react with an attack of bronchial asthma upon an intoxicating dose of the poison (Meltzer). Babcock recalls the case of a sufferer from asthma who was operated upon for gall-stones, with relief of the asthma, and as long as drainage of the gall-bladder was maintained there was no asthma, but with stoppage of drainage it returned; finally, with cure of the gall-bladder the asthma disappeared. Likewise the removal of nasal polyps restores drainage to the accessory sinuses of the nose and relieves a pent-up focus of absorption which has been causing attacks; the removal of hypertrophied turbinates acts in the same way. In some cases the smell of horses or of the stable in a sensitized individual will bring on an attack. Sometimes the injection of horse serum even in the form of antitoxin will produce an attack;[4] a friend of mine who received a small immunizing dose of diphtheria antitoxin had such a severe anaphylactic reaction with asthma that his life was despaired of. Asthmatic attacks occurring with hay fever, and due to the pollen of rag weed, golden rod,[5] etc., are of the same origin; inoculation with constantly increasing emulsions

[3] Vaughan, V. C.: Proteid Split Products in Immunity and Disease.

[4] Sturtevant, Mills: Serum Sickness in a Series of 500 Patients Treated with Diphtheria Antitoxin, Arch. Int. Med., vol. xvii, No. 1.

[5] Gottleib and Oppenheimer: Active Immunization in Hay Fever, Biochemical Bull., New York, 1915, No. 4, p. 127.

of these pollens, or polyvalent emulsions, will cure or improve the attacks. Egg proteid also causes attacks in some individuals. I have in mind a child who had asthmatic attacks after eating eggs, and which attacks cleared up after a change in diet. The urticaria following the ingestion of fish is of the same character; likewise the urticaria following the injection of antitoxin.

Another source of attack (and one with which I have been working) is due to the presence of bacteria, primarily Streptococcus viridans or Streptococcus hemolyticus, secondarily Micrococcus catarrhalis.[6] These cases are obviously infective, and the more asthma I see the larger I think this group is; they occur with bronchitis, and sometimes run an acute course with febrile reaction, increase in pulse rate, cough, and sputum, and are often followed by emphysema.

If the sputum be collected in a sterile cup or Petri dish, washed, and a loop stirred in blood agar and poured in a Petri dish, and later streaked on North's medium, streptococcus can practically always be grown. Whatever the variety of germ, whether Streptococcus viridans or Streptococcus hemolyticus, an autogenous vaccine will cure the attacks. It is best given twice a week, in constantly increasing strength, for twelve to twenty injections. It is much better to give such dosage that local reaction occurs, although I have had cures in patients who showed no local reaction. On the other hand I have had cases which showed no improvement until doses were given in sufficient quantity to cause local reaction. I have adopted the practice of beginning with 100,000,000 in adults and feeling my way cautiously until finding the dose that caused local reaction, and then provoking a local reaction on every injection. If at any time the local reaction be too severe, or if general symptoms occur in the form of fever, chilliness, general malaise or aches, or increase in the asthma, I allow a rest for a period before beginning again, using my judgment as to continuing the same dosage or dropping back to a smaller one; it is better to avoid going backward if possible. 1000 million is often far enough to carry them, although more obstinate cases may require 2000 million, and I have carried them to 3000 million and higher. It is very striking to see the asthma clear up after the first injection, as has happened in a number of my cases. The longest period of cure I have to report is two years. I have been struck with the fact that streptococcus seems to be the chief offender; one case which had very foul sputum, and who showed Bacillus Friedländer, had to leave town, so that I had no opportunity of vaccinating him. I have had no pneumococcus cases. Micrococcus catarrhalis, I am convinced, is usually a mouth infection in asthma. I do not find it often in sputum that is carefully washed, and when the specimen for culture is carefully selected. Vaccination by catarrhalis seems to have had very little action on the asthmatic attacks when mixed infection

[6] Allen, R. W.: Vaccine Therapy and Opsonic Treatment.

is present. Babcock reports excellent results in a case of mixed infection, in which he used a mixed vaccine of pneumococcus, streptococcus and an anaërobic bacillus.[7] After inoculation for a time at semiweekly intervals it is usually advisable to make the intervals weekly.

In analyzing the following cases several facts are striking.

1. Clearing up of the asthma after the first or second injection (Cases 2, 3, 4, 6, 12, 14).

2. Cases that progressively improved from the time vaccines were started (Cases 1, 9, 14, 15).

3. Cases that did well but had occasional short relapses (Case 5, much improved, but could not continue treatment); case 10.

4. Obstinate cases which were finally cured (case 7) or improved (case 8).

5. Unimproved, case 11 (tuberculosis).

6. Of the 16 cases, 12 were cured, 3 were improved, and only 1 unimproved (tuberculosis).

7. Twelve cases required from 9 to 16 injections, extending over a period of from four to eleven weeks. Two cases were given treatments of fifteen and seventeen weeks respectively.

I should advise always using the regular vaccine or tuberculin syringe divided into hundredths, as no accurate count can be made with the ordinary hypodermic syringe, especially when small volumes are given. The following cases will show the preparation and method of administration of the vaccine, and the result of treatment:

Case I.—L. B. R., aged six years. December 18, 1914. The child has had various attacks of bronchitis associated with asthma since nine months of age; attacks coming on at intervals of a few weeks and lasting from two to four days, accompanied by cough, dyspnea, temperature, sleepless nights, and loss of weight; they were harassing to the child and a cause of much anxiety on the part of the parents. As treatment had but slight and temporary effect, a swab was made from the larynx during an attack, and Gram-positive cocci obtained, which were arranged in long chains; on blood agar these colonies were each surrounded by an area of hemolysis. Vaccines were prepared and administered as follows:

Dec. 18.	Streptococcus hemolytic	5,000,000.	No reaction.		
23.	" "	10,000,000.	Temperature	100.6	
30.	" "	25,000,000.	"	100.4	improved.
Jan. 6.	" "	50,000,000.	"	100.6	"
13.	" "	75,000,000.	"	100.0	"
20.	" "	100,000,000.	"	100.0	"
28.	" "	125,000,000.	"	100.0	"
Feb. 5.	" "	150,000,000.	"	100.0	cured.
10.	" "	175,000,000.	"	100.4	"
19.	" "	200,000,000.	"	100.6	"
24.	" "	250,000,000.	"	100.4	"
Mar. 3.	" "	300,000,000.	"	100.4	"
9.	" "	350,000,000.	"	100.4	"

Cured; at the present writing (February, 1916) the child has had no further attacks, and is perfectly well.

[7] Journal of the American Medical Association, vol. lxiv, No. 26.

December, 1916. This patient has relapsed and is again under treatment.

CASE II.—Charles Spanze, aged twenty-five years; Italian; fruit vendor February 15, 1915.

No alcoholic nor venereal history. For four months has had attacks of asthma, every three or four weeks, lasting two or three days each and interfering with sleep. He had two hemoptyses three months ago, has lost seven pounds, and has had a few night sweats. Physical examination reveals no positive signs of tuberculosis, but chest is filled with squeaking rales and gives the signs of emphysema. Sputum examination shows no tubercle bacilli; Gram stain shows positive cocci in the washed sputum, and poured sputum reveals Streptococcus viridans in blood agar; vaccines were made from this and administered as follows:

Feb. 15.	Streptococcus viridans.	50,000,000.	Slight local reaction.	No asthma after this first injection.
18.	" "	100,000,000.	Slight local reaction.	
21.	" "	300,000,000.	" " "	
24.	" "	500,000,000.	" " "	
27.	" "	600,000,000.	" " "	
Mar. 3.	" "	700,000,000.	" " "	
6.	" "	800,000,000.	" " "	
9.	" "	900,000,000.	" " "	
12.	" "	1,000,000,000.	" " "	

On March 12 he was discharged cured, having gained four pounds. A letter from him five months later stated he had had no return of his asthma.

On October 5, seven months after discharge, he was back complaining of cough, slight difficulty in breathing, but no distinct asthma. Sputum was again examined; showed no tubercle bacilli; Gram-negative cocci, in pure culture, vaccines were again made and administered.

Oct. 22.	Micrococcus catarrhalis.	100,000,000.	Slight local reaction.
25.	" "	200,000,000.	" " "
29.	" "	300,000,000.	" " "
Nov. 2.	" "	400,000,000.	" " "
5.	" "	600,000,000.	" " "
9.	" "	800,000,000.	" " "

During these three weeks his attacks became more frequent and of greater severity, so that 500 million streptococci were added to the vaccine with the result of a severe local reaction, chilliness, and temperature 102°, but with a cessation of the asthma. Sputum was again ordered and cultured, when pure Streptococcus viridans were grown on blood agar, and vaccines prepared.

Nov. 12.	Micrococcus catarrhalis.	1,000,000,000.	Intense local and general reactions; temperature 102°, chilliness; severe local reaction; no more asthma.
	Streptococcus viridans.	500,000,000.	
16.	Micrococcus catarrhalis.	1,200,000,000.	
	Streptococcus viridans.	700,000,000.	
23.	Micrococcus catarrhalis.	1,300,000,000.	Injections at weekly intervals. No asthma; marked local reactions.
	Streptococcus viridans.	700,000,000.	

No more catarrhalis were given, as they seemed to do no good when patient was getting them alone.

30.	Streptococcus viridans.	700,000,000.	No asthma; marked local reaction.
Dec. 7.	" "	800,000,000.	" " " " "
14.	" "	1,000,000,000.	" " " " "
21.	" "	2,000,000,000.	By mistake. " " "
Jan. 11.	" "	2,250,000,000.	No asthma; " " "
18.	" "	2,250,000,000.	" " " " "
25.	" "	2,200,000,000.	" " " " "

Discharged cured; has gained three pounds more. An urticarial eruption followed the last injection. Had he been put on viridans at the beginning instead of catarrhalis, I doubt if he would have had any return. One month later he had gained four pounds more, a gain of fifteen pounds since starting treatment and he felt perfectly well.

CASE III.—L. Wilson, aged thirty-three years, conductor. April 1, 1915.

His mother has had asthma for forty years. He has no alcoholic nor venereal history.

His first attack of asthma was two months ago, lasting thirty hours, after which it disappeared for five weeks; since that time it has been fairly continuous, with choking and coughing in the morning and difficult breathing at night; the cough has been very harassing.

Physical examination shows an overacting heart, 104. Lungs give slight comparative dulness at the right apex, with slightly prolonged and high-pitched expiration; there are sibilant rales over all. Weight, 125 pounds.

Sputum shows many Gram-positive cocci, some in clumps and some in chains. No tubercle bacilli; sputum poured in blood agar gives Streptococcus viridans. Vaccines were given as follows:

Apr. 15.	Streptococcus viridans.		50,000,000.	Slight reaction.	
18.	"	"	100,000,000.	" "	
21.	"	"	200,000,000.	Moderate "	
24.	"	"	300,000,000.	" "	
27.	"	"	500,000,000.	" "	
30.	"	"	700,000,000.	" "	
May 3.	"	"	800,000,000.	" "	There was no return of the asthma after the first injection.
6.	"	"	900,000,000.	" "	
9.	"	"	1,000,000,000.	" "	

Discharged cured May 9, "feeling better than for the past two years;" weight 131 pounds, a gain of 13 pounds. In August of the same year he reported no return, and in February of the following year he reported continued cure.

CASE IV.—Celia Jaffe, aged twenty-eight years, October 22, 1915.

This patient had attacks of asthma in childhood until fourteen years of age. It returned seven months ago at intervals of three or four days, lasting one or two nights each time. Cough only recently; no hemoptyses; no sweats; no loss of weight.

Physical examination shows a well-nourished woman, breathing labored, with scattered sibilant and sonorous rales.

Sputum shows many Gram-positive cocci, no tubercle bacilli. Blood agar shows Streptococcus viridans.

Oct. 30.	Streptococcus viridans.		200,000,000.	No local reaction.	
Nov. 4.	"	"	400,000,000.	" " "	No asthma.
7.	"	"	600,000,000.	" " " " "	
10.	"	"	800,000,000.	" " " " "	
13.	"	"	1,000,000,000.	Good " " " "	
16.	"	"	1,100,000,000.	" " " " "	
20.	"	"	1,300,000,000.	" " " " "	
24.	"	"	1,300,000,000.	" " " " "	
27.	"	"	1,300,000,000.	Several local and general reaction so none was given for two weeks.	
Dec. 11.	"	"	1,300,000,000.		
21.	"	"	1,500,000,000.	No asthma; severe itching of the skin, but nothing to be seen.	

Discharged cured December 21.

CASE V.—James Burk, aged twenty-five years; sailor. November 5, 1915.

Not alcoholic. Eighteen months ago had cough and pain in the chest; mucopurulent sputum; could not work for three weeks; cough and sputum were worse in the morning; he lost 35 pounds, but is now gaining. While at sea he is well, but on shore his breathing is affected by bad weather, and he has wheezing and dyspnea.

Physical examination shows a well-built and well-nourished man, with hyper-resonant chest and with sibilant and sonorous rales; no localized signs.

Sputum shows Gram-positive and Gram-negative cocci; blood agar, Streptococcus viridans; no tubercle bacilli. Vaccines were given as follows:

Nov. 10	Streptococcus viridans.	100,000,000.	No reaction; no asthma.
13.	" "	200,000,000.	" " " "
16.	" "	300,000,000.	" " " "
20.	" "	500,000,000.	" " slight oppression.
23.	" "	800,000,000.	" "
27.	" "	1,200,000,000.	Severe attack with advent of severe easterly storm; no return of asthma. As he had to go to sea he was now discharged improved, "by his own statement feeling very much better;" the severe attack with the advent of the easterly storm was the only attack after injections were started.
30.	" "	1,500,000,000.	
Dec. 3.			

CASE VI.—Meyer Grisham, aged twelve years, school. November 10, 1915.

For some months has had attacks at night, so that he had to sit up out of bed to breathe; attacks were at intervals of a few days.

Physical examination negative except for asthma.

Culture showed Gram-positive and Gram-negative cocci. Streptococcus viridans on blood agar. No tubercle bacilli. Vaccines as follows.

Nov. 13.	Streptococcus viridans.	100,000,000.	Severe local reaction.
	Micrococcus catarrhalis.	100,000,000.	
16.	Streptococcus viridans.	200,000,000.	" " " no asthma.
	Micrococcus catarrhalis.	200,000,000.	
20.	Streptococcus viridans.	300,000,000.	" " " " "
	Micrococcus catarrhalis.	300,000,000.	
27.	Streptococcus viridans.	400,000,000.	Moderate " " " "
30.	" "	500,000,000.	" " " " "
Dec. 3.	" "	600,000,000.	" " " " "
7.	" "	700,000,000.	Good " " " "
18.	" "	700,000,000.	Slight; weekly injections now.
21.	" "	800,000,000.	Good local reaction.
28.	" "	1,000,000,000.	

Discharged, December 28, cured; no attacks since treatment was begun.

CASE VII.—Emma Wilson, aged sixty years; dressmaker. November 30, 1915.

Father died of tuberculosis; patient has one son who had asthma and who was cured by inoculation (see Case III). At the age of eighteen years patient had asthma and hay fever, which attacks

recurred every year; twenty years ago she moved from the country to New York City, when the hay fever disappeared but the asthma continued, and increased to such an extent that attacks were at intervals of a few days. Upon returning to the country in the summer the hay fever would return. Asthma, however, has been nearly continuous for years.

Physical examination shows a well-nourished woman with scattered sibilant and sonorous rales and labored breathing.

Sputum gave no tubercle bacilli, but Gram-positive cocci in clumps, the isolated ones being in chains. On blood agar, streptococcus grew in pure cultures. Vaccines were given as follows:

Nov. 30.	Streptococcus viridans.		100,000,000.	No reaction; no improvement.
Dec. 4.	"	"	300,000,000.	No reaction; bad asthma with storm.
7.	"	"	500,000,000.	Slight reaction; improved, slight asthma.
11.	"	"	750,000,000.	Slight reaction; still has asthma.
14.	"	"	1,000,000,000.	Moderate reaction; improvement after this.
21.	Seven	days.	1,250,000,000.	" " one attack since last.
28.	Seven	"	1,500,000,000.	" " oppression but no real asthma.
Jan. 8.	Eleven	"	1,500,000,000.	Moderate reaction; no asthma, feels better.
25.	Seventeen	"	1,500,000,000.	" " well until two days ago, slight attack.
Feb. 1.	"	"	1,500,000,000.	Moderate reaction; no asthma.
5.	"	"	1,600,000,000.	" " " "
12.	"	"	2,000,000,000.	" " " "
16.	"	"	2,250,000,000.	" " " "
23.	"	"	2,500,000,000.	" " " "

Discharged, cured, February 23.

This was a case of many years' standing and proved obstinate. Patient was irregular in her attendance, but after improvement began it was continuous, and was followed by complete cure.

CASE VIII.—Nita Connolly, aged twenty-five years; colored; domestic. For two years has had attacks at biweekly intervals, oppressed breathing, with cough and expectoration.

Physical examination negative except for asthmatic breathing.

Sputum showed no tubercle bacilli; Gram-positive cocci which proved to be Streptococcus viridans on blood agar. Vaccines were given as follows:

Nov. 27.	Streptococcus viridans.		100,000,000.	Not autogenous.
Dec. 11.	"	"	100,000,000.	" " improved.
21.	"	"	250,000,000.	Autogenous; "
Jan. 3.	"	"	300,000,000.	Good reaction.
8.	"	"	500,000,000.	Good reaction; one attack.
15.	By mistake.		2,700,000,000.	Marked reaction; local and general; no asthma.
22.	"		1,700,000,000.	Marked reaction; no asthma.
Feb. 5.	"		1,700,000,000.	Moderate reaction; mild attack with grippe.
11.	"		2,000,000,000.	Not autogenous; no asthma.
15.	"		2,000,000,000.	No asthma.
22.	"		2,500,000,000.	No asthma.

This girl was irregular in attendance and obstinate in reaction, but was greatly improved.

CASE IX.—Charles Clement, aged eight years, November 25, 1915. Cough and colds for one year; indisposition to play; no loss of weight; no hemoptyses; no sweats; never well. One year ago was seen by Dr. F. L. Keays, who diagnosed bronchopneumonia; but

the signs of this cleared up. The child, however, has remained listless and half sick. Various consultations have been held upon him, with the result that no positive diagnosis of tuberculosis could be made, and no tubercle bacilli have been found in the sputum after repeated examinations. Recently he has complained of pain in the back, and examination revealed a dorsal kyphosis, with spasm and pain upon motion. Asthma has existed over the entire period, which greatly harasses him and interferes with sleep. I saw him in consultation December 1, and on examination he revealed the dorsal kyphosis and well-defined signs of cavity in his left upper lobe. I took this to be a bronchiectatic cavity following his bronchopneumonia. Sputum examination showed no tubercle bacilli, but a culture of Streptococcus viridans and Staphylococcus albus. I made a vaccine of this and sent it to Dr. Keays, who administered it as follows:

Dec.	5.	Streptococcus viridans.	35,000,000.	No reaction; no result.
		Staphylococcus albus.	35,000,000.	
	8.	Streptococcus viridans.	70,000,000.	
		Staphylococcus albus.	70,000,000.	" " " "
	12.	Streptococcus viridans.	140,000,000.	
		Staphylococcus albus.	140,000,000.	" " " "
	16.	Streptococcus viridans.	280,000,000.	
		Staphylococcus albus.	280,000,000.	Sleeps better; less asthma.
	19.	Streptococcus viridans.	560,000,000.	
		Staphylococcus albus.	560,000,000.	
	23.	Streptococcus viridans.	800,000,000.	Improved.
	26.	" "	1,200,000,000.	"
	30.	" "	1,500,000,000.	" slight local reaction.
Jan.	2.	" "	1,500,000,000.	" " " "
	6.	" "	1,500,000,000.	" " " "
	9.	" "	1,500,000,000.	" " " "
	13.	" "	1,500,000,000.	No asthma; sleeps well.
	16.	" "	1,800,000,000.	" " " "
	20.	" "	1,800,000,000.	" " " "
	27.	" "	1,800,000,000.	
Feb.	3.	" "	2,000,000,000.	

Entirely cured of asthma, sleeps all night and is very much more comfortable; of course he has his original condition, and Dr. Keays is inclined to think he has sarcoma of the lung. This boy was a very unpromising case, and I hesitated to undertake his cure, but he did remarkably well. I heard from him two months later, and he was still free from asthma.

Case X.—J. S., aged twenty-one years. January 20, 1916.

Various attacks for a period of one year, coming on at intervals of two or three weeks at first, but latterly they have been continuous.

Physical examination shows only labored breathing, with whistling rales. Sputum shows no tubercle bacilli, but Streptococcus viridans and Micrococcus catarrhalis. Vaccines were given as follows:

Feb.	1.	Streptococcus viridans.	210,000,000.	Improved; no reaction.
	5.	" "	300,000,000.	" less cough.
	8.	" "	400,000,000.	" local reaction.
	12.	" "	800,000,000.	" marked local.
	15.	" "	1,000,000,000.	Bad attack with very cold weather.
	19.	" "	1,250,000,000.	Much better.
	24.	" "	2,250,000,000.	No asthma; moderate reaction.
Mar.	2.	" "	2,500,000,000.	" " " "

This boy reported great improvement. As he thought himself well he stopped coming, and I feel sure has had no return.

CASE XI.—Nellie B., aged thirty years; housewife. November 30, 1915.

For years had cough; dyspnea; smothering, especially at night. During last pregnancy the attacks cleared up six months before confinement and appeared three weeks after.

Physical examination shows a pale thin woman whose lungs are filled with sibilant and sonorous rales; at the right apex are slight dulness and subcrepitant rales. Sputum shows no tubercle bacilli, but Streptococcus viridans in blood agar.

This woman was vaccinated for two months twice a week, and carried as high as 3100 million without the slightest benefit. She stopped coming of her own accord, so I had no chance of increasing the doses further.

The following cases are loaned me through the courtesy of Dr. T. W. Hastings.

CASE XII.—Miss B. G. T., aged 41 years. June 13, 1914.

Had hay fever for fourteen years; asthmatic attacks, including horse asthma, with cough and expectoration. She was in Saranac in 1914, with supposed tuberculosis. Culture now made of the sputum, and Streptococcus viridans and Micrococcus albus isolated. Vaccines were given as follows:

Aug. 20.	{Streptococcus viridans.	120,000,000.	Worse for three days following.
	{Micrococcus albus.	60,000,000.	
25.	" "	240,000,000.	No asthma.
	" "	120,000,000.	
Sept. 1.	" "	360,000,000.	Slight local reaction.
	" "	180,000,000.	
8.	" "	480,000,000.	No asthma.
	" "	240,000,000.	
24.	" "	600,000,000.	"
	" "	300,000,000.	
Oct. 7.	" "	720,000,000.	"
	" "	360,000,000.	
18.	" "	840,000,000.	"
	" "	420,000,000.	
Nov. 1.	" "	960,000,000.	"
	" "	480,000,000.	
10.	" "	1,200,000,000.	"
	" "	600,000,000.	

Discharged, cured, November 10. No attacks after the second injection.

CASE XIII.—Miss E. U., aged eighteen years; school. April 15, 1910.

For years had cough and wheezy breathing and real asthmatic attacks, especially at night; sputum culture showed Streptococcus and Micrococcus catarrhalis. Vaccines were given as follows:

Apr. 30.	{Streptococcus pyogenes.	66,000,000.	Mild local reaction.
	{Micrococcus catarrhalis.	60,000,000.	No reaction; no asthma.
May 10.	" "	132,000,000.	No asthma.
	" "	132,000,000.	
18.	" "	165,000,000.	" "
	" "	165,000,000.	
26.	" "	165,000,000.	" "
	" "	165,000,000.	
31.	" "	225,000,000.	Moderate local reaction.
	" "	225,000,000.	No asthma.
Jan. 4.	" "	225,000,000.	" "
	" "	225,000,000.	
10.	" "	330,000,000.	" "
	" "	330,000,000.	

Discharged, cured, January 10. No attacks since treatment started.

CASE XIV.—Mrs. O. H. February 11, 1915.

A sufferer from asthma for years; no tuberculous element present. Sputum showed Gram-positive and negative cocci; no tubercle bacilli present. Vaccines were administered as follows:

Mar. 18.	{Streptococcus viridans. {Micrococcus catarrhalis.	100,000,000. 50,000,000.	
22.	" "	200,000,000. 100,000,000.	
26.	" "	300,000,000. 150,000,000.	
30.	" "	400,000,000. 200,000,000.	No local but slight local reaction.
Apr. 3.	" "	500,000,000. 250,000,000.	" " " " "
7.	" "	600,000,000. 300,000,000.	" " " " "
11.	" "	700,000,000. 350,000,000.	" " " " "
15.	" "	800,000,000. 400,000,000.	" " " " "
19.	" "	900,000,000. 450,000,000.	" " " " "
23.	" "	1,000,000,000. 500,000,000.	Slight local; no asthma.
28.	" "	800,000,000. 400,000,000.	" " "
May 2.	{Streptococcus viridans. {Micrococcus catarrhalis.	1,000,000,000. 500,000,000.	
6.	" "	1,200,000,000. 600,000,000.	Severe local reaction.
10.	" "	1,400,000,000. 700,000,000.	" " "
17.	" "	1,600,000,000. 800,000,000.	" " "
24.	" "	1,800,000,000. 900,000,000.	Marked " "
June 1.	" "	1,800,000,000. 900,000,000.	" " "
8.	" "	2,000,000,000. 1,000,000,000.	Slight " "
15.	" "	2,200,000,000. 1,100,000,000.	
22.	" "	1,600,000,000. 800,000,000.	
30.	" "	2,000,000,000. 1,000,000,000.	
July 8.	" "	2,400,000,000. 1,200,000,000.	
16.	" "	2,800,000,000. 1,400,000,000.	
23.	" "	3,200,000,000. 1,600,000,000.	
30.	" "	3,600,000,000. 1,800,000,000.	
Aug. 6.	" "	4,000,000,000. 2,000,000,000.	
13.	" "	4,400,000,000. 2,200,000,000.	
20.	" "	4,800,000,000. 2,400,000,000.	
27.	" "	5,200,000,000. 2,600,000,000.	

There was only one attack of asthma since beginning treatment. Injections were followed within a few hours by very mild attacks, but were of no consequence and of only focal character. She reports great improvement and feels better than she has felt for years. Cured.

CASE XV.—Lieut. B., U. S. A., aged twenty-nine years. January, 1910.

Ever since childhood has had attacks of bronchitis and asthma. In 1907 he had an operation on his turbinates, with vaccines, and was cured. For the past two weeks he has had shortness of breath

at night, but no true asthma. Physical examination shows sibilant and sonorous breathing, but no local signs. Sputum was cultured and vaccines made of equal parts of Streptococcus hemolyticus and Micrococcus catarrhalis.

Jan.	14.	Streptococcus hemolyticus	and	Micrococcus catarrhalis.	27,000,000	each.
	18.	"	"	"	54,000,000	"
	21.	"	"	"	81,000,000	"
	25.	"	"	"	108,000,000	"
	28.	"	"	"	135,000,000	"
Feb.	1.	"	"	"	162,000,000	"
	8.	"	"	"	198,000,000	"
	15.	"	"	"	216,000,000	" weekly intervals.
	25.	"	"	"	243,000,000	each ten day intervals.
Mar.	7.	"	"	"	270,000,000	each.

The following case does not belong strictly to this class, but I enter it as a matter of interest as belonging to a spasmodic group like asthma.

CASE XVI.—P. L. C., aged eleven years; school. October 30, 1914.

Has always been subject to attacks of coryza and sore throat accompanied by spasmodic laryngitis. Tonsillectomy five years ago with only moderate results. He lost fifty-five days' schooling the past year, owing to frequent colds. Recently had a severe coryza and bronchitis, with spasmodic cough. Physical examination was negative. Sputum cultured. Streptococcus viridans and Micrococcus albus grown; no tubercle bacilli found. Vaccines were given as follows:

Nov.	23.	Streptococcus viridans.	25,000,000.	
		Micrococcus catarrhalis.	10,000,000.	
Dec.	2.	"	"	37,000,000. Local for twenty-four hours.
		"	"	15,000,000.
	14.	"	"	50,000,000.
		"	"	20,000,000.
	18.	"	"	62,000,000.
		"	"	25,000,000.
	21.	"	"	75,000,000.
		"	"	30,000,000.
Jan.	4.	"	"	100,000,000.
		"	"	40,000,000.
	8.	"	"	125,000,000.
		"	"	50,000,000.
	11.	"	"	150,000,000. No reaction.
		"	"	60,000,000.
	18.	"	"	250,000,000.
		"	"	100,000,000.
	22.	"	"	300,000,000.
		"	"	150,000,000.
	27.	"	"	350,000,000.
		"	"	175,000,000.
Feb.	1.	"	"	400,000,000.
		"	"	200,000,000.
	8.	"	"	400,000,000.
		"	"	200,000,000.
	15.	"	"	400,000,000. Coryza for two weeks; no reaction.
		"	"	200,000,000.
Mar.	1.	"	"	400,000,000.
		"	"	200,000,000.
	8.	"	"	450,000,000.
		"	"	225,000,000.
	18.	"	"	500,000,000.
		"	"	250,000,000.

Bronchitis much improved; there has been no return of the spasmodic laryngitis.

I wish to express my thanks to Dr. T. W. Hastings, for his kind assistance, also to Dr. W. C. Thro for many valuable suggestions.

THE EFFECT OF ANESTHESIA AND OPERATION ON KIDNEY FUNCTION AS SHOWN BY THE PHENOLSULPHONEPHTHALEIN TEST AND URINARY ANALYSIS.

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The following is a report of the effect of anesthesia and operation on kidney function as demonstrated by the phenolsulphonephthalein test and urinary analysis performed on 55 cases, selected mainly because of the objections raised to disturbing unnecessarily those cases which were to undergo or had undergone operations for involved intra-abdominal conditions.

The series comprises: 22 cases of hernia, 11 cases of chronic appendicitis, 6 cases of gynecological surgery, 3 cases of varicose veins, 3 cases of hemorrhoids, 3 cases of nephritic origin, 7 miscellaneous cases, as cholecystectomy, gastrectomy, cervical lymphadenectomy, hydrocele, sarcoma of the leg, carcinoma of the breast, and an orchidectomy. The cases were operated upon by the second surgical division of the Presbyterian Hospital.

The Routine. The routine followed was to have the patient drink four glasses of water, usually at fifteen minute intervals, so as not to cause nausea, and then at the end of the hour previous to the injection, have him void so as to insure the emptyness of the bladder. One cubic centimeter of the phthalein dye was then injected subcutaneously into the triceps region of the arm, and a sample of urine taken every few minutes until the characteristic red color appeared in the urine which had been previously rendered alkaline by the addition of a few drops of a 25 per cent. solution of sodium hydroxide. The time of the first appearance was noted and the urine excreted, collected for that hour, and the succeeding one, in separate bottles. The usual technic of diluting the specimen to 1 liter after it has been alkalinized was followed, and a sample read as soon as possible by the Helliges colorimeter by artificial light, it having been found that the matching of the intensity of color was better made thereby.

In cases in which doubt existed as to bladder retention the patient was always catheterized; in fact, 30 of the 33 males were catheterized at the end of the second hour, and whenever the color did not appear in fifteen minutes, a catheter was introduced, provided that there was urinary retention. The 22 female cases were all catheterized, the catheter being left in the urethra until the test was completed. About thirty-six hours after operation a second injection was made, the only exception being that sometimes the patient was unable to drink the full four glasses of water because of its nauseating effect after operation and anesthesia.

In addition a twenty-four hour specimen of urine was collected before operation and one after, an attempt being made to secure a better view of the activity of the kidney. The specimen was measured and described, its reaction and specific gravity noted, an albumin test performed, and a portion centrifuged and examined especially for casts.

The Anesthetic. The anesthesia employed was ether in 47 cases, given by the Bennet inhaler, previous to which a bag of nitrous oxide was administered; gas and oxygen in 7 cases given by the Luke apparatus; local anesthesia in 1 case with novocain 1 per cent.

THE AVERAGE PHTHALEIN EXCRETION.

In 47 ether cases the average ante-operative phthalein was	57.9 per cent.
Average p. o. phthalein	57.3 per cent.
Decrease	.6 "
In the 7 gas and oxygen cases the average ante-operative phthalein was	52.2 per cent.
Average p. o. phthalein was	49.0 "
Decrease	3.2 "

The Urine Analysis. The urine analysis showed 15 cases having albumin, 2 of which showed casts, or albumin present in 27 per cent. of the cases; of these 10 showed albumin after operation, 6 with casts. Ten cases, previously negative, developed albumin after operation, practically every one of these cases showing many hyaline and finely granular casts, or 25 per cent. of the previously negative urines showed some passing effect of kidney irritation.

EFFECT OF LENGTH OF ETHER ANESTHESIA AND OPERATION ON KIDNEY FUNCTION.

8 anesthesias lasting fifteen to twenty-nine minutes:	
Average a. o. phthalein	52.3 per cent.
Average p. o. phthalein	58.5 "
Increase	6.2 "
2 cases showed a trace of albumin with casts (postoperative).	
10 cases lasting thirty to forty-four minutes:	
Average a. o. phthalein	58.8 per cent.
Average p. o. phthalein	58.8 "
No change.	
4 cases showing albumin, 3 with casts (postoperative).	
11 cases lasting forty-five to fifty-nine minutes:	
Average a. o. phthalein	58.4 per cent.
Average p. o. phthalein	57.1 "
Decrease	1.3 "
7 cases showing albumin, 5 with casts (postoperative).	
11 cases lasting sixty to seventy-four minutes:	
Average a. o. phthalein	58.8 per cent.
Average p. o. phthalein	57.9 "
Decrease	.9 "
4 cases showing albumin, 1 with casts (postoperative).	

4 cases lasting seventy-five to eighty-nine minutes:

Average a. o. phthalein	50.8 per cent.
Average p. o. phthalein	40.8 "
Decrease	10.0 "

3 cases showing albumin with casts (postoperative).

Showing probably that as the length of anesthesia is prolonged the functional activity of the kidney is depressed, while in the shorter cases there is practically no change, perhaps even a mild degree of stimulation.

EFFECT OF AGE AND ANESTHESIA ON KIDNEY FUNCTION.

Below 20 years, average a. o. phthalein	64.1 per cent.	p. o. 61.5 per cent.
Below 20 to 39 years, average a. o. phthalein	56.0 "	p. o. 57.3 "
Below 40 to 59 years, average a. o. phthalein	52.8 "	p. o. 51.8 "

Showing mainly that as the age in years increases that the threshold activity of the kidney is diminished.

Effect of Type of Patient and Anesthesia on Kidney Function. That the kidney is affected by psychic influence and individual variation is well known, and it is partially illustrated in the figures given below.

I. Normal or average type:	
a. o. phthalein	58.7 per cent.
p. o. phthalein	59.8 "
Increase	1.10 "
II. Nervous type:	
a. o. phthalein	60.5 per cent.
p. o. phthalein	56.0 "
Decrease	4.5 "
III. Obese type, which, as a rule take anesthesia very poorly with cyanosis:	
a. o. phthalein	56.6 per cent.
p. o. phthalein	44.9 "
Decrease	11.7 "
IV. Anemic type:	
a. o. phthalein	55.5 per cent.
p. o. phthalein	46.0 "
Decrease	9.5 "
V. Arteriosclerotic type:	
a. o. phthalein	53.5 per cent.
p. o. phthalein	50.7 "
Decrease	2.9 "

The Ether Cases Individually. While the averaged case of ether anesthesia shows but little change the cases considered individually vary considerably one way or the other.

Twenty-two cases showed an increased postoperative phthalein of about 11 per cent. Ante-operative urine examination was negative in 17 of these cases and pathological in 5 cases or 22 per

cent., these 5 cases showing albumin but no casts. The postoperative urine examination of this series was negative in 15 cases, pathological in 7 cases, 3 cases previously having no abnormality now showing albumin, 1 with hyaline casts.

Twenty-two cases showed a decreased postoperative phthalein of about 16 per cent. average. The anteoperative urine examination was negative in 13 of these cases; pathological in 9 or 41 per cent.; 7 of these cases showing a faint trace of albumin, 2 with casts, and 2 cases showing a heavy trace of albumin and no casts. Postoperative urine examination of this series was negative in 8 cases, pathological in 14, 6 cases of the 9 already mentioned showing further changes, 3 cases showing a greater albumin reaction, 4 cases now for the first time showing casts. Eight cases previously showing no urinary change now showed pathological elements, 1 case with a faint trace of albumin with casts, 4 cases with a moderate trace of albumin, 1 with casts, and 3 cases with a heavy trace of albumin, all with casts.

Within this group were 2 cases of nervous temperament which gave no urinary change, but marked phthalein postoperative deficiency; 1 other case was especially cyanotic, and had previously had Magendie solution ℥vj, leaving 2 cases which showed a decreased postoperative phthalein with no explanation or rather an attempt at one.

While the series of cases is small, it seems reasonable to suppose that preëxisting conditions of albuminuria predispose to a lowering of kidney efficiency as shown by the phthalein test after operation and anesthesia; and that in the majority of cases showing a decrease output, there is an accompanying urinary picture showing the effects of kidney irritation, rather mild in nature. That this is not permanent, is shown by a third phthalein test in 5 of the cases which suffered a severe depression, where in ten days time the kidney output was practically restored to what it was originally, and the urine examination was once more negative, or in the condition it was, before anesthesia.

The Gas and Oxygen Cases. Although there were but 7 cases of gas and oxygen, they show very interesting results.

In 2 cases of anesthesia of thirty-five and forty-five minutes respectively with an ante-operative phthalein of 51 per cent., and a postoperative phthalein of 47 per cent., a decrease of 4 per cent. occurred; one of the patients was of the nervous type and the other was a case of cardiovascular disease.

There were 4 cases of anesthesia of sixty, sixty-six, seventy, and a hundred and ten minutes with the average ante-operative phthalein excretion of 54 per cent., and a postoperative phthalein of 54 per cent., showing in one case only a faint trace of albumin after operation.

The seventh case was an anesthesia of a hundred and fifty minutes

with a decreased output postoperative of 14 per cent., the urine showing a trace of albumin and many hyaline casts.

Comparing this with the results obtained from ether anesthesia, in 3 of the cases which were very nervous, the average ante-operative phthalein was 55 per cent., the postoperative phthalein, 54 per cent., or a difference of 1 per cent. as compared with the difference of 4.5 per cent. in the ether series of nervous patients.

SUMMARY AND CONCLUSIONS. Upon the whole, the average case after thirty-six hours postoperative shows very little change in kidney function as demonstrated by the phenolsulphonephthalein test, although 25 per cent. showed urinary changes, which in ten days time were again negative.

The functional activity of the kidney is depressed as the length of anesthesia is increased, while in short anesthesias the kidney might even appear to be stimulated to a slight degree.

As age increases the threshold activity of the kidney is lessened.

Nervous patients, anemic, obese, and arteriosclerotic patients as a rule, show some effect of their physical or psychic state on kidney function.

Preëxisting conditions of albuminuria have a tendency to decreased phthalein excretion, and those cases which have a decreased phthalein excretion, in the majority of instances, show effects of kidney depression as evidenced by careful urinary analysis, although these effects are only temporary.

For long anesthesias and apparently for nervous patients, gas and oxygen as an anesthetic seems to have the least irritating effect on kidney function, as demonstrated especially by urine examination.

AN UNUSUAL DISORDER OF THE CARDIAC MECHANISM RELIEVED BY SURGICAL OPERATION.

BY EDWARD B. KRUMBHAAR, M.D., PH.D.

PHILADELPHIA.

(From the Medical Division of the Hospital of the University of Pennsylvania, Philadelphia, Pa.)

FROM the two points of view the following case is of interest, as an example, (1) of an unusual type of disordered mechanism of the heart beat, and (2) of the efficacy of removing cryptic or frank sources of reflex damage to the cardiac mechanism.

History. A. R., a married woman, aged fifty-six years, was admitted to the surgical wards of the University Hospital for repair of cystocele and rectocele. On physical examination, however, the pulse was found to be so distinctly irregular that the operation was

postponed. The following pertinent facts were obtained from the past history and examination:

The patient has never had any cardiac symptoms further than slight attacks of palpitation for several years, associated with indigestion and flatulence. For the past two years she has noticed some slight dyspnea on exertion, but never any edema or chronic cough. She did not know that her pulse was irregular. The pelvic symptoms—pain in right side of abdomen and a palpable mass in the vagina—have been present for two years. She has had four healthy children and one miscarriage (probably from overexertion). Aside from the coupled beats and pelvic disorders, physical examination revealed nothing of importance. The heart was of average size and the sounds normal. At times there was a pulse deficit of 50 per cent., due to the second beat of each couple failing to reach the wrist, but this beat was always sufficient to raise the aortic valves. There was no congestion, edema, or other signs of myocardial weakness. The urine showed a normal specific gravity, a faint trace of albumin, but no casts. Blood examinations were negative.

An electrocardiogram taken at this time revealed (Fig. 1) a condition of coupled beats, that on superficial examination might be mistaken for nodal rhythm coupled with regularly recurring extrasystoles arising from a part of Tawara's node other than that responsible for the nodal rhythm. The arrhythmia was later considered, however, to be due to auricular extrasystoles coupled with normal beats, both being followed by an unusually short conduction time. The basis for these interpretations will be discussed later. The atropin test (2 mgms. hypodermically) failed to affect the "coupled" rhythm, although the cardiac rate was raised from 92 to 118 beats per minute. Digitalis medication (0.67 c.c. of the tincture four times a day) succeeded after six days in lengthening the *P-R* interval to 0.16 second, but the premature contractions continued to appear almost constantly in the form of "pulse bigeminus."[1] (It is perhaps noteworthy that the *P-R* interval of the first cycle of each pair began to lengthen after three days of digitalis, whereas the second cycle required eight more doses before it was affected.)

As the arrhythmia had been found not to be of serious import, the contemplated surgical operation was performed with uneventful success. The pulse-rate did not go beyond 106 at any time during the operation, and was noted as regular during the period of anesthetization. This regularity continued during convalescence, and an electrocardiogram taken at that time showed that a normal mechanism existed (Fig. 2). As the influence of digitalis wore off the shortening *P-R* interval did not return to its former position beyond

[1] The influence of digitalis on the form of the T-wave (Cohn, Jour. Exp. Med., 1915, xxi, 593) is fairly well demonstrated in this case.

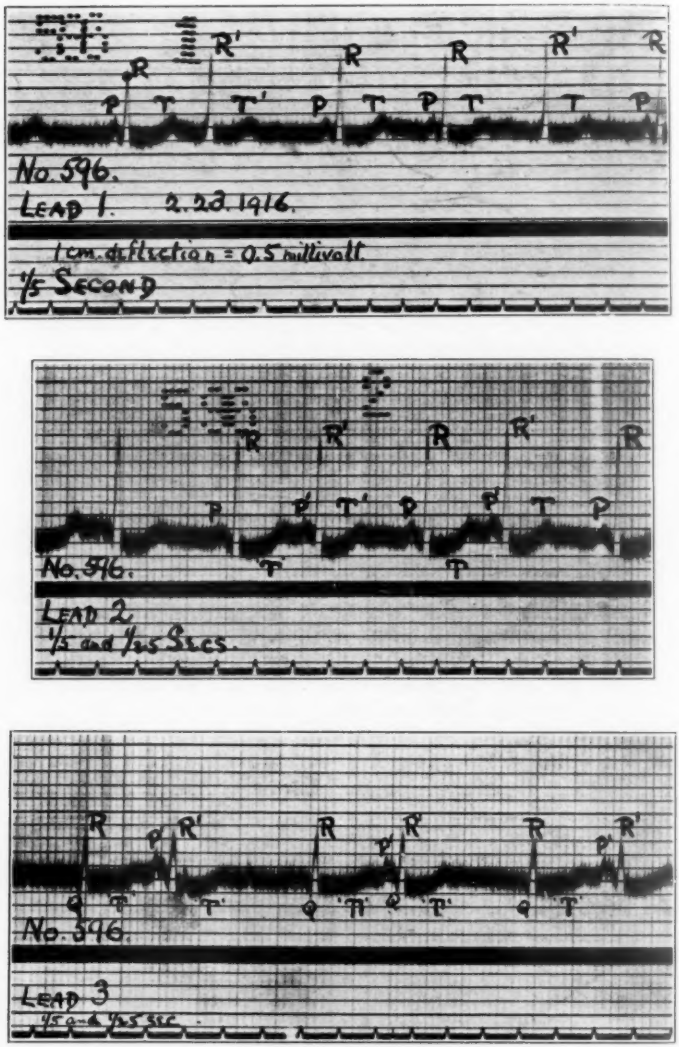

FIG. 1.—Electrocardiograms from the three customary leads, showing shortened *P-R* interval and "pulsus bigeminus," due to recurring auricular extrasystoles. Note that the *P* of the second cycle of each pair is of slightly different form from that of the first. In Lead 1 the ectopic P-wave and in Lead 3 the normal P-wave are not plainly distinguishable, but were present in other records taken during the period of bigeminy. The *P-R* interval is 0.10 and 0.09 second respectively. (Normal *P-R* interval 0.12 to 0.17 second.)

the shorter normal limits, and when the patient was last seen the ectopic beats had not reappeared. The patient continued in good

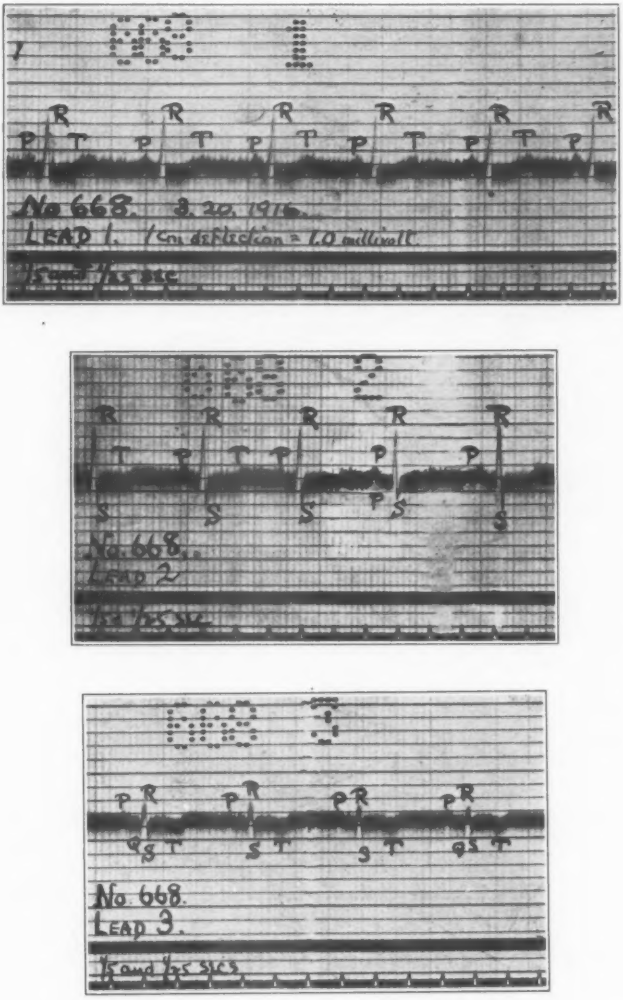

FIG. 2.—Electrocardiograms showing normal rhythm. Note absence of ectopic beats and that the *P-R* interval is now within normal limits (0.12 second).

health, gained weight, and during the period of observation had no cardiac symptoms of any kind. It is regrettable that the patient

cannot return for future study, so that it is impossible now to say whether or not the return of the cardiac mechanism to normal rhythm has proved permanent.

The preliminary interpretation of nodal extrasystoles added to nodal rhythm was based on the very short *P-R* intervals (0.10 and 0.09 second), thus fulfilling one of the two necessary requirements for the diagnosis of ectopic beats arising in Tawara's node,[3] namely, either that auricle and ventricle should contract simultaneously or that the conduction time should be distinctly shortened (normal *P-R* interval being 0.12 to 0.17 second). The other requirement—that *P*, the sign of auricular activity, should be of altered form—is only imperfectly shown in the second beat of each pair and not at all in the first. (The nervous condition of the patient rendered it impossible at any time to obtain records free from tremors.) In several cases in the literature a rhythm made up of cardiac cycles similar to the first one of each of these records has been called "nodal rhythm," in spite of the fact that Lewis and others have shown that impulses arising at an appreciable distance from the sinus node cause diphasicity or inversion of the *P* wave. A case recently observed at the Presbyterian Hospital of New York[4] demonstrates that at least some cases of apparent nodal rhythm with upright *P* are in reality due to a prolonged *P-R* interval equal in length to the interval of a cardiac cycle, so that *P* of one cycle falls on *R* of the preceding cycle. Whether true nodal rhythm can occur without obvious changes in the form of *P* is a point that is well worth studying experimentally.

In the present case, however, the gradual lengthening of the *P-R* interval under the influence of digitalis without change in the form of *P*, proves that the unusually short *P-R* interval of both cycles was due not to ectopic impulses arising in Tawara's node, but to lessened conduction time of impulses arising in the sinus node and an ectopic site in the auricle respectively. As the chief factor in the production of the *P-R* interval is the delay caused by the passage of the impulse through Tawara's bundle,[5] one must assume that the shortened interval of this case was due to positive dromotropic influences on this structure, and that these influences disappeared with repair of the pelvic disorders, as did the bathmotropic influences that caused the auricular extrasystoles. About the possible causes of such an increased conductivity, however, there is practically no evidence at hand, either clinical or experimental.

SUMMARY. A case of cardiac arrhythmia is described in which a condition of ectopic beats arising in different parts of Tawara's node was simulated by a shortened conduction time (*P-R* interval) with recurring auricular extrasystoles (pulsus bigeminus).

[3] Lewis, Thomas: Clinical Electrocardiography, p. 50.
[4] Personal communication from Dr. Strong.
[5] Hering, H. E.: Arch. f. d. ges. Phys., 1909–1910, cxxxxi, 572.

Both of these disorders of the cardiac mechanism were relieved by a pelvic operation (anterior and posterior colporrhaphy), at least to the extent that they disappeared during the period of observation.

My thanks are due to Dr. C. C. Norris for permission to study this case.

LEAD POISONING IN CHILDREN WITH ESPECIAL REFERENCE TO LEAD AS A CAUSE OF CONVULSIONS.[1]

By Kenneth D. Blackfan, M.D.,
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We are indebted to the Australian writers Gibson, Love, Turner, Breinl and Young and others for much of the recent literature regarding lead poisoning in children. They have had an unusually good opportunity to study this condition. Thus, in the Brisbane Children's Hospital, 76 cases were seen in five years and Gibson himself observed 24 cases in six years.

I shall not attempt to give a complete review of the literature on the subject, as the chief object of this communication is to draw attention to lead as a cause of convulsions in children and to report 4 cases seen in Dr. Howland's clinic at the Harriet Lane Home, the Johns Hopkins Hospital. For the more important articles, the reader is referred to those from which I have freely quoted.[2]

The symptoms of lead poisoning vary according to the susceptibility of the child and to the duration of the infection. The degree of susceptibility is variable. Breinl and Young refer to many instances in which only one child in a family was affected, although the other children were exposed to the same influences. In other instances, one child reacted with pronounced symptoms while the only evidence of infection in the others was a blue line on the gums.

Gibson[3] considers the ingestion of lead as the most likely source of infection, although he appreciates that it may occur from the inhalation of dust containing lead. He points out that children

[1] From the Harriet Lane Home, Johns Hopkins Hospital, and the Department of Pediatrics, Johns Hopkins University.

[2] Gibson, Love, Hardie, P. Bancroft, Jeffris Turner: Notes on Lead Poisoning as Observed in Children in Brisbane, Intercolonial Medical Congress of Australasia, Sydney, 1892, p. 76. Gibson, Lockhart: Ocular Neuritis Simulating Basal Meningitis Plumbism, Australasian Med. Gaz., October 20, 1897, p. 479. A Plea for Painted Railings and Painted Walls of Rooms as the Source of Lead Poisoning Among Queensland Children, Australasian Med. Gaz., 1904, xxiii, 149. The Importance of Lumbar Puncture in the Plumbar Ocular Neuritis of Children, Tr. Australasian Med. Congress, 1911, ii, 750. Breinl and Young: The Occurrence of Lead Poisoning Among North Queensland Children, Ann. Trop. Med. and Parasitol., 1914–15, viii, 475. Turner, Jeffris: Lead Poisoning Among Queensland Children, Australasian Med. Gaz., 1897, October 20, p. 475.

[3] A Plea for Painted Railings and Painted Walls of Rooms as the Source of Lead Poisoning Among Queensland Children, Australasian Med. Gaz., 1904, xxiii, 149.

who bite their fingernails and suck their fingers are much more frequently affected, and believes that their hands became contaminated with dried paint from porch railings and houses. That poisoning may occur through inhalation has been shown by the experiments of Goadby and Goodbody[4] and by Legge and Goadby.[5] They conclude that the danger from inhalation is far greater than from the ingestion of lead. While this, no doubt, is true among workers in lead, the swallowing of lead in some form is probably the more common source of the poisoning in children.

In the early cases a change in disposition is often the first symptom which is noticed. The child becomes fretful, peevish, and often very restless at night. The appetite becomes poor, the breath foul, and frequently hemorrhages occur from the gums. The child may complain of pain in the epigastrium and legs.

In the cases of longer duration the pains in the abdomen become continuous and more severe. Constipation is present, as a rule. Vomiting rarely occurs. The muscles are often so painful as not to permit of the weight of the bed-clothing. The gait of the patients is described as being characteristic. It is a waddling gait; they walk on the outside of the feet, the toes are dragged, and with each step the legs are swung sideways before the feet are put to the ground. Occasionally the parents' attention may be attracted by one or more of the many indefinite signs enumerated above, but not infrequently nothing abnormal is noticed until the development of cerebral disturbances. The cerebral manifestations will be referred to later.

Very few of the cases reported by Breinl and Young showed the characteristic wrist-drop so common in adults. This has been the experience of others, and generally the paralysis first affects the legs in children. A paralysis much like that of the Aran-Duchenne type occurring in muscular dystrophy has been reported in 2 cases. Paralysis of the cranial nerves is very common; the facial and the motor oculi nerves, either entire or in part, are those most frequently involved.

Gibson[6] has reported a most interesting group of eye symptoms which he refers to as a "plumbic ocular neuritis." The neuritis usually occurs in children below the age of eight years. There may be an optic neuritis, with retinal hemorrhages, or an optic atrophy. There is an accompanying weakness of one or both external recti muscles. He has seen as many as 9 such cases in a year, but in the 22 cases reported by Breinl and Young only 1 patient was so affected.

[4] Seventh International Congress of Applied Chemistry, 1909, Section VIIIa, 306.
[5] Poisoning and Lead Absorption, London, 1912, p. 122.
[6] Ocular Neuritis Simulating Basal Meningitis Plumbism, Austral. Med. Gaz., October 20, 1897, p. 479. The Importance of Lumbar Puncture in the Plumbic Ocular Neuritis of Children, Tr. Austral. Med. Congress, 1911, ii, 750.

The temperature is, as a rule, normal, though it may be irregularly elevated. In the fatal cases, and especially those with cerebral disturbances, it may be high, reaching 105° or 106° before death.

Very often the clinical symptoms are not sufficient to warrant a diagnosis of lead poisoning. This is especially true in the early cases. However, when there are suggestive symptoms other evidences of the condition are usually to be found. Among these are the blue line on the gums and stippling of the red cells. Basophilic granulations are present in a small number of red blood corpuscles in the majority of the cases. The blood otherwise shows nothing characteristic, although there may be a secondary anemia. This apparently is determined by the duration of the poisoning.

Direct evidence of lead poisoning is obtained by the demonstration of lead in the urine or feces. In this connection the recent observations of Breinl and Young are most interesting. They examined eight children with early signs of the disease, *i. e.*, slight pains in the epigastrium and legs, but without basophilic granulations and the lead line, and found appreciable quantities of lead in the excreta. They found there was always a larger amount in the feces than in the urine, and that it was often present in the feces when it could not be demonstrated in the urine. Dixon Mann[7] found larger quantities of lead present in the feces than in the urine. Others have made this observation, and Legge and Goadby say that lead in the urine is not so common nor definite a symptom as supposed.

From the foregoing summary of the more common clinical signs seen in lead poisoning in children it is evident that a definite classification of the cases into different groups is difficult, and when made has to be based on the severity of the predominating symptom. For instance, one patient may present the characteristic picture of the disease, one may show only irritability and indefinite pains in the abdomen, whereas another may become paralyzed or may be seized with convulsions while in apparent health. In spite of the difficulties attendant upon establishing a classification for lead poisoning, Jeffris Turner[8] speaks of four main groups as follows:

1. Paralytic cases showing symmetrical wrist-drop and foot-drop; spasm of the calf muscles, and as a secondary lesion, a persistent talipes equinus; (2) cases characterized by pains in the abdomen and limbs, concomitant with habitual constipation, and an occasional blue line on the gums, the children becoming at the same time irritable and neurotic; (3) children suffering from ocular neuritis, a neuritis involving the optic, and at the same time the oculomotor nerves; (4) eclamptic cases suffering from severe and persistent convulsions which often end fatally.

In the cases reported from Australia, convulsions were observed

[7] Forensic Medicine and Toxicology, London, 1908, p. 487 (C. Giffin & Co.).

[8] Lead Poisoning Among Queensland Children, Australasian Med. Gaz., October 20, 1897, p. 475.

very infrequently, though mild cerebral disturbances were frequently present. That convulsions may occur in the course of lead poisoning, has been recognized since the observations of Stockhausen[9] in the seventeenth century. The first careful investigation of the cerebral disorders due to lead was made by Tanquerel.[10] He grouped them under the term Encephalopathia Saturnina. Though his researches were published in 1882, but little attention has been paid to the lead encephalopathies except as they are found in adults and in particular among workers in lead. Lead as a cause of convulsions in children has been ignored almost entirely, and especially among observers in this country.

An interesting and extensive series of cases with convulsions has been reported by Stewart,[11] They occurred among 64 cases of lead poisoning which he investigated in Philadelphia, due to eating buns colored with chrome yellow. Seven of the 16 cases in which convulsions occurred were in children between one and a half years and twelve years of age. Stewart believed that of the various forms of cerebral disorders produced by lead, the convulsive was by far the most common—that it formed two-thirds, if not more, of all the cerebral manifestations, and that it had the highest mortality. He (Stewart) thought it impossible to make any clinically exact systematic grouping of the different forms of the lead encephalopathies as Tanquerel[12] did, as one form merges into the other.

Stewart cites 2 cases of so-called idiopathic epilepsy which were secondary to convulsions, symptomatic of lead poisoning, and suggested that epilepsy of lead origin may be of much more frequent occurrence than is generally supposed.

The macroscopic changes most frequently found in the brain are an edema and anemia, with flattening of the convolutions. The brain may, however, be markedly congested. There is often a thickening of the pia—it may be adherent to the cortex. There may be hemorrhages into the pia and between the pia and the cortex. There is also a round-cell infiltration within the pia, and the neuroglia cells of the cortex are found to be increased. Spiller[13] observed a proliferation of the endothelial cells upon the surface of the cerebral pia. Such pathological findings may occur in other conditions, and similar lesions may be found in patients with lead poisoning who have not manifested cerebral symptoms.

There is no way by which the convulsive seizures *per se* in lead poisoning can be distinguished from those due to other causes. All types of convulsions are seen. They may be local or general.

[9] Quoted by Stewart (see nbte 11).
[10] Lead Diseases (translation by Dana, 1848), p. 263.
[11] Lead Convulsions, Am. Jour. Med. Sc., 1895, cix, 288.
[12] Tanquerel established the following divisions: (1) delirious forms; (2) comatose form; (3) convulsive forms; (4) above forms combined.
[13] Jour. Med. Research, 1903, x, No. 1.

They may be mild or severe. The convulsions in lead poisoning do, however, have certain peculiarities which appear to be characteristic of the disease. They are very persistent, they show a great tendency to recur, and they are attended by a high mortality.

The persistence of the convulsions is shown in Cases II and III. Enormous doses of bromides, chloral, and morphin were administered to each patient without causing any effect on the convulsions. It was only by the continued use of chloroform that they could be controlled, and when this was discontinued the convulsions began anew. In one patient (Case I) there were two recurrent attacks in a period of seven and a half months. The convulsions recurred after a period of eighteen days in another patient (Case II). With each recurrent attack they were severe, and were controlled only with chloroform. One patient (Case III) died in the first convulsive attack. The convulsions in one patient (Case IV) were mild, lasting only one day. He was delirious at first, then had convulsions, after which he was comatose for several days. The behavior of this patient serves to support Stewart's contention that it is not possible to define sharply the encephalopathies into definite groups.

The high mortality of convulsions due to lead is shown by Stewart's cases. The termination was fatal in 6 of the 7 children. A series of most remarkable cases reported by Berger[14] emphasizes the fatality of the condition equally well. In a pot-glazier's family, who lived day and night in an atmosphere saturated with lead fumes, the father suffered from the comatose variety of lead encephalopathy. Seven children died in convulsions, four others had frequent cerebral disorders and suffered from peripheral neuritis. Several of the grandchildren died in convulsions. In my series of cases 3 of the 4 patients died. The patient who recovered has not shown any evidences of a recurrence. One patient (Case I) died in convulsions during the third attack, another (Case II) during the second attack, and the other (Case III) during the first attack.

The temperature, which was normal on admission in two patients (Case II and Case III), preceding death rose to 107.5° and 105.5° respectively. Such a hyperpyrexia has been present preceding death from lead convulsions in most of the reported cases.

Evidences of cerebral involvement other than convulsions were present. In one patient (Case I) there was rigidity of the neck and a positive Kernig sign. He had also a paralysis of the left external rectus muscle of the eye. Another patient (Case IV) had rigidity of the neck and a temporary paralysis of the facial nerve.

Mosny and Malloizel[15] and Plate [16] and others have pointed out that there is very generally evidence of involvement of the meninges,

[14] Berl. klin. Wchnschr., 1874.

[15] La meningite saturnine, 1907, xxvii, 506.

[16] Ueber einen Fall von Meningitis saturnina, München. med. Wchnschr., 1913, lx, 2343.

as shown by the fact that the cerebrospinal fluid contains an increased number of cellular elements. In chronic lead poisoning they rarely found any change in the cerebrospinal fluid. In this series the spinal fluid from all the patients was examined and changes were found in three of them. In these three patients the spinal fluid was clear, not under increased pressure, and a fibrin clot did not form on standing. In two patients (Case II and Case III) the cellular elements were not increased, but there was a marked globulin reaction (Ross-Jones). In one patient (Case I) there were thirty cells per cubic millimeter, mainly lymphocytes, and a marked globulin reaction. The spinal fluid from this patient was examined on several occasions over a period of eight months, and on each examination there was an increase in cells and a positive globulin. In the fourth patient (Case IV) the spinal fluid was not examined until four weeks after he had recovered, and at this time it showed no changes other than twelve cells per cubic millimeter. Such a slight increase in cells does not signify a pathological change.

Eye changes during the course of lead encephalopathies have been noted by a number of different observers. Wilbrand and Sanger,[17] who have collected reports of most of the cases, believe that optic neuritis may occur primarily through the direct toxic action of lead on the nervous system or by the production of interstitial neuritis or through the alterations of the bloodvessels in the retina and optic nerves. It also may occur secondarily through intracranial changes or changes in the kidney. Gibson, as mentioned previously, has written extensively on the eye changes in children, and believes that they frequently occur without other symptoms of lead poisoning. In two of my patients (Case I and Case II) there were extensive hemorrhages into the retina and optic neuritis. In one (Case I) the condition gradually subsided and the eye grounds became normal after a month. At the time of his second admission there were retinal hemorrhages and a choked disk. The eye grounds were normal in the other two patients (Cases III and IV).

As a rule there are certain symptoms which precede the development of the convulsions. These may be the common symptoms of plumbism or they may be so slight as to escape notice. Colic has been more frequently observed than paralysis or arthralgia, but more common are irritability, restlessness, and a blue line on the gums. Vomiting and constipation are not infrequent, and many patients complain bitterly of pain in the head. In two patients (Case I and Case IV) of this series there was an interval of several days before the convulsions, when the children were irritable during the day and restless at night. One of them complained of headache, and they both had attacks of vomiting. In one instance (Case III) the indefinite symptoms covered a period of about three months. There

[17] Die Neurologie des Auges, 1913, vol. v.

was evident impairment of general health with frequent attacks of vomiting and colic. At times the onset of convulsions is sudden.

The duration of the period between the first exposure to lead and the development of cerebral symptoms is variable. The exact time of the exposure in the patients of this series could not be determined with certainty. Three of them (Cases I, II and III) had been exposed for many months, as the source of the infection was found to be from eating paint. In one patient (Case IV) the source of lead was not ascertained.

In addition to the symptoms preceding the convulsions the patients in this series showed other evidences of lead poisoning. The blood picture was that of a moderate secondary anemia, and in all a few red blood corpuscles showed basophilic degeneration. In the four patients there was a leukocytosis of about 20,000, with a moderate increase in the polymorphonuclear cells. The blue line on the gums was present in three of the four patients (Cases I, III, IV). It should be remembered that a continuous lead line is seldom found. The characteristic appearance is the presence of minute black dots in the margin of the mucous membrane around the teeth which are covered with tartar. It is difficult to see and without the aid of a hand lens may readily be overlooked.

Efforts made to determine lead in the urine of two patients (Cases I and II) were unsuccessful. The feces were not examined.

The following are brief histories of the 4 cases which form the basis for this report:

Case I.—The patient, W. M.,[18] aged five and one-half years, complained first of pain in his head, and was very restless at night. The following day he vomited several times, and it was noticed that his neck was stiff. He appeared very ill, became rapidly worse, and on the fourth day of his illness severe generalized convulsions began. On the fifth day, August 22, 1913, he was brought to the hospital in a comatose state. He continued to have recurrent generalized convulsions, his neck was retracted, and there was an internal strabismus of the left eye. There was an optic neuritis and a hemorrhagic retinitis on the right. The left optic nerve was normal. The temperature was normal. The leukocytes were 27,600. The spinal fluid obtained on four occasions was clear and sterile. It was under slightly increased pressure at the first spinal puncture, but subsequently the pressure was normal. There were from twenty to forty cells per cubic centimeter (mostly mononuclears). The Noguchi globulin reaction was positive. The Wassermann (blood) was negative. The convulsions ceased after the first lumbar puncture, but he remained in coma for the next two days. He gradually improved and after a week seemed nearly well. The convulsions did not recur and he was discharged

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September 20, 1913. The abnormal changes in the right optic nerve gradually subsided, but the spinal fluid contained an increase in cells and a positive globulin reaction. With the exception of an occasional attack of vomiting and abdominal pain, he remained in excellent condition for five months.

On March 1, 1914, he complained of headache and he vomited. The convulsions recurred, and on March 3 he was again admitted to the hospital. His condition was almost identical with that at the time of the first admission. There were generalized and persistent convulsions, a definite rigidity of the neck, and an optic neuritis and hemorrhagic retinitis of the right eye. At this examination the characteristic lead line was seen on the gums. The red blood corpuscles were 4,480,000, the white blood corpuscles 23,000, and the hemoglobin 55 per cent. There was well-marked stippling of the red blood corpuscles (Grawitz granules). No lead could be demonstrated in the urine. The convulsions subsided after lumbar puncture. Two or three days after admission an internal strabismus of the right eye developed. The patient made an uneventful recovery and was discharged on May 1.

He remained in apparently good health for three weeks, when on May 25 he had a severe convulsion and died. No postmortem examination was obtained. The source of the lead was determined when his lips were found covered with white lead paint which he had nibbled from the railings of his crib. On investigation at the orphanage where he lived it was found that the white paint on his bedstead had been entirely gnawed off.

Case II.—R. B. (7094). This patient was aged two and one-half years. On March 8, 1915, he had a convulsion which lasted about two hours. From then until March 12 he seemed well. On the morning of March 12 convulsions began about 7.30. He was brought to the hospital at noon the same day in convulsions, which continued for about twenty-four hours. These convulsions involved the eyes, the left side of the face, and the left arm. He had no fever. There was a leukocytosis of 19,000. The red blood cells were 4,000,000. Hemoglobin, 50 per cent. There was well-marked stippling of the red cells.

On examination the positive findings were a lead line about the upper and lower teeth and an enlarged spleen. He was entirely relaxed between the convulsions, the reflexes were not exaggerated, and Kernig's sign was absent. The eye grounds were normal. The spinal fluid was clear and not under pressure. There were seven cells per cubic millimeter and a positive globulin reaction. Examination of the urine for lead was negative.

The child had no convulsions in the hospital, and was discharged on March 25. He was brought back to the hospital on March 26, twelve hours after discharge, in a convulsion which involved the face and the left arm. He continued to have convulsions for twenty-four

hours in spite of energetic treatment with morphin, chloral, and bromides. By the administration of chloroform the convulsions could be checked, but they recurred as soon as it was discontinued. The temperature rose to 107.5° just before death.

Source of Lead. The father stated that the child would gnaw any painted article, and that he and his brother had recently ruined a set of parlor furniture by eating the paint from it.

CASE III.—(9182) H. B., aged two years. A brother (R. B., Case No. II) died in the Johns Hopkins Hospital of lead poisoning March 27, 1915.

The patient was a normal child, and was well until he had varicella at sixteen months. Shortly after this he complained of pain in the abdomen and was operated on by an orthopedist for appendicitis (February, 1915). The appendix was normal. For two or three months preceding the onset of his acute illness he was not well. He often vomited and complained a great deal of abdominal pain. He vomited more than usual on October 15, 1915, and at 11 P.M. had a convulsion. The convulsions continued, and he was admitted to the hospital the following day, October 16. The patient was comatose on admission and was having repeated and severe convulsions. The convulsions were general in character, with possibly greater involvement of the right than the left side of the body. The neck was not rigid; there was no Kernig's sign. The knee-kicks were not obtained. Examination of the mucous membrane about the teeth failed to show a lead line.

Ophthalmoscopic Examination. Right: The margin of the disk was obscured. The vessels were full and tortuous; there were small retinal hemorrhages. Left: The margin of the disk was obscured by a large retinal hemorrhage, and there were other hemorrhagic areas throughout. The leukocytes were 20,000. The red blood cells were 3,600,000 and the hemoglobin was 55 per cent. Many stippled red cells were present. The spinal fluid was clear and not under increased pressure. There were nine cells per cubic millimeter and the reaction for globulin was positive.

Course in Hospital. The convulsions persisted in spite of enormous doses of chloral and morphin. It was only possible to control them by the use of chloroform. This, however, was of temporary benefit, as the convulsions commenced again when it was discontinued. The patient did not regain consciousness. The temperature, which was 97.6° on admission, gradually rose, and just before death reached 105.5° (fifteen hours after admission).

Source of Lead. Same as in Case II.

CASE IV (8491).—J. N., aged three years. The patient, the older of two children, was of normal development and, with the exception of pertussis at two years, had always been well. There was no history of convulsions. The present illness began acutely on July 30, 1915, with drowsiness. He slept the greater part of that

day, was very weak, refused his food, and vomited. At night he was delirious. He jumped out of bed, cried out several times, and threw his head back as though in pain. The next day, July 31, he appeared better, though still weak and drowsy. Again, at night, he became delirious and had several attacks of crying and throwing his head back. On August 1 he was comatose, and he had several convulsions. He did not improve, and was admitted to the hospital August 2.

The temperature on admission was 101°, pulse 124, respirations 20. He lay quietly in bed, with his eyes closed, and made no effort to speak. He was well-nourished and did not appear very ill. The neck muscles were slightly rigid and attempts to flex the neck caused pain. The reflexes were active but not increased. The examination of the heart and lungs was negative. The spleen was palpable. There was a well-marked lead line present in the mucous membrane about several of the upper teeth. It was especially well defined about the upper lateral incisors. The optic discs were normal.

The red blood corpuscles showed stippling in a few cells. The white blood corpuscles were 7500 per cu.mm. The differential count was:

	Per cent.
Polymorphonuclears	67
Small mononuclears	20
Large mononuclears	6
Transitionals	2
Polymorphonuclear eosinophiles	5

The Wassermann (blood) was negative.

Course in the Hospital. The child lay in a semistupor for most of the day after his admission. He was easily aroused, and at times appeared conscious but would not speak. The respirations were full and deep, varying between eighteen and twenty-four. They were irregular, and a few periods of apnea were observed. There was a well-marked tâche cérébrale, and Kernig's sign was suggestive. The neck was rigid. The condition remained the same for the next two or three days. There were no convulsions. On August 5 the patient seemed much better. He sat up in bed and could walk when placed on his feet. On this day an incomplete paralysis of the right facial nerve was observed. Improvement in his condition continued. The temperature gradually became normal, and six days after (August 8) admission he appeared quite well, except that he was very weak. The facial paralysis slowly became less marked, and it disappeared after about ten days. When he was discharged on August 12 (ten days after admission) he was apparently well.

A lumbar puncture was made several times during his stay in the hospital, but blood was obtained each time, and for this reason a cytological examination was not made. Four weeks after the onset,

when the child was apparently well, the spinal fluid was clear, not under increased pressure, and contained twelve cells per cubic millimeter. The globulin reaction at this time was positive. The source of lead was not determined.

Case.	I.—W. M. 2 years.	II.—H. B. 2½ years.	III.—R. B. 2 years.	IV.—J. N. 3 years.
Onset of convulsions	4th day	1st day	2 to 3 mos.	3 days.
Leukocytes	27,600	20,000	19,000	19,500
Spinal fluid:				
Cells	30	9	7	12 [19]
Globulin	+	+	+	0
Temperature, on admission	99.4° F.	99° F.	97.6° F.	101° F.
Lead line	+	0	+	+
Stippling red blood cells	+	+	+	+
Eye	Hemorrhagic retinitis; choked disk	Same as Case I	Negative	Negative.
Neurological	External rectus palsy; convulsions; coma; rigidity of neck	Convulsions; coma	Convulsions; coma	Delirium; convulsions; coma; rigidity of neck; facial paralysis.
Source of lead	Eating paint	Eating paint	Eating paint	Not known.
Result	Died	Died	Died	Well at present time.

Conclusions. In conclusion, I would urge that energetic prophylactic measures be taken with children who habitually eat painted articles in order to guard against the development of lead poisoning. Since my attention has been directed to lead poisoning I have found a number of children who nibble the white paint from enameled cribs.

In all patients with convulsions in which the etiological factor is not clear, lead should be suspected. This can be readily determined, as in the majority of instances there are other evidences of the condition, *e. g.*, the lead line, basophilic degeneration, and the presence of lead in the feces.

The examination of the spinal fluid may prove to be an index as to the seriousness of the affection and of prognostic aid. In three of the four patients changes were found. In one patient (Case I) changes were present in the spinal fluid for many months, and the patient eventually succumbed. In another patient (Case IV) who has recovered, and in whom the convulsions were not severe, the spinal fluid could not be examined at the time of the convulsions. Four weeks later the spinal fluid contained twelve cells and the globulin reaction was normal.

[19] Four weeks after the convulsion.

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Polymorphonuclear eosinophiles	5

The Wassermann (blood) was negative.

Course in the Hospital. The child lay in a semistupor for most of the day after his admission. He was easily aroused, and at times appeared conscious but would not speak. The respirations were full and deep, varying between eighteen and twenty-four. They were irregular, and a few periods of apnea were observed. There was a well-marked tâche cérébrale, and Kernig's sign was suggestive. The neck was rigid. The condition remained the same for the next two or three days. There were no convulsions. On August 5 the patient seemed much better. He sat up in bed and could walk when placed on his feet. On this day an incomplete paralysis of the right facial nerve was observed. Improvement in his condition continued. The temperature gradually became normal, and six days after (August 8) admission he appeared quite well, except that he was very weak. The facial paralysis slowly became less marked, and it disappeared after about ten days. When he was discharged on August 12 (ten days after admission) he was apparently well.

A lumbar puncture was made several times during his stay in the hospital, but blood was obtained each time, and for this reason a cytological examination was not made. Four weeks after the onset,

when the child was apparently well, the spinal fluid was clear, not under increased pressure, and contained twelve cells per cubic millimeter. The globulin reaction at this time was positive. The source of lead was not determined.

Case.	I.—W. M. 2 years.	II.—H. B. 2½ years.	III.—R. B. 2 years.	IV.—J. N. 3 years.
Onset of convulsions	4th day	1st day	2 to 3 mos.	3 days.
Leukocytes	27,600	20,000	19,000	19,500
Spinal fluid:				
Cells	30	9	7	12 [19]
Globulin	+	+	+	0
Temperature, on admission	99.4° F.	99° F.	97.6° F.	101° F.
Lead line	+	0	+	+
Stippling red blood cells	+	+	+	+
Eye	Hemorrhagic retinitis; choked disk	Same as Case I	Negative	Negative.
Neurological	External rectus palsy; convulsions; coma; rigidity of neck	Convulsions; coma	Convulsions; coma	Delirium; convulsions; coma; rigidity of neck; facial paralysis.
Source of lead	Eating paint	Eating paint	Eating paint	Not known.
Result	Died	Died	Died	Well at present time.

Conclusions. In conclusion, I would urge that energetic prophylactic measures be taken with children who habitually eat painted articles in order to guard against the development of lead poisoning. Since my attention has been directed to lead poisoning I have found a number of children who nibble the white paint from enameled cribs.

In all patients with convulsions in which the etiological factor is not clear, lead should be suspected. This can be readily determined, as in the majority of instances there are other evidences of the condition, *e. g.*, the lead line, basophilic degeneration, and the presence of lead in the feces.

The examination of the spinal fluid may prove to be an index as to the seriousness of the affection and of prognostic aid. In three of the four patients changes were found. In one patient (Case I) changes were present in the spinal fluid for many months, and the patient eventually succumbed. In another patient (Case IV) who has recovered, and in whom the convulsions were not severe, the spinal fluid could not be examined at the time of the convulsions. Four weeks later the spinal fluid contained twelve cells and the globulin reaction was normal.

[19] Four weeks after the convulsion.

PRIMARY ENDOTHELIOMA OF THE PLEURA.

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PHILADELPHIA.

(From the McManes Laboratory of Pathology, University of Pennsylvania.)

The purpose of this paper is to report in full a case of endothelioma of the pleura. I am indebted to Dr. Alfred Stengel for permission to use the case, and the very excellent history is the product of his staff at the University Hospital. I may be forgiven for including considerable detail in the pathological protocol in view of the fact that the condition is not rare but relatively uncommon and the opportunities for studying the cases in full have evidently not been numerous.

In reviewing the records of the pathological department, comprising over 5000 reports, I have found 9 cases, a report of which will appear later. According to Clarkson, out of 10,000 autopsies in the Pathological Institute at Munich, only 2 cases of primary endothelioma were found. He obtained from the literature 41 cases. I have made no attempt to cover all of these cases, but in reviewing a few of them several points may be noted: There has been some confusion between the primary sarcoma and primary endothelioma, and in some cases this is merely in the use of terms. The older writers are meager in their descriptions, but they mention the resemblance to carcinoma, so that by some the term "endothelial cancer" is used. It would seem that the growth occurs either as one large mass, usually posterior in position, infiltrating the lung, or as several small nodules, confined to and scattered over the pleura. Both pleuræ are involved, often with dense adhesions, and fluid. Metastases are common but not widespread. The diagnosis before autopsy is always difficult, with the possibility of tuberculosis and aneurysm as factors. Absence of temperature and negative sputum, with progressive dyspnea, weakness, loss of weight, and signs pointing to consolidation in the chest without pain, seem to be the predominating factors from the records I have been able to consult.

Case History.—J. M., white, American, salesman, was admitted to the University Hospital April 4, and died April 30, 1914. He complained of loss of weight, weakness, and constipation. His present illness began sixteen months ago with a vomiting spell. This was not accompanied by pain. Dizzy attacks soon followed. Six months later he noticed a loss of voice, a hacking, nonproductive cough, belching of gas, and vomiting every day after meals. He then began to progressively grow weaker, with loss of weight. During the past ten months he has lost forty pounds. For the past month night sweats have been constant, with a cough now associated with expectoration of a mucopurulent character. He

sleeps poorly, his appetite is failing, is constipated, and requires cathartics.

The patient stated that his father died of tuberculosis and one brother of Bright's disease. He denied syphilis, and has always been well until his present attack.

It was noted upon physical examination that he was amaciated, with a pale, warm, moist and sallow skin. The superficial lymph nodes were palpable. The radial pulses were equal, synchronous, and of good volume and tension. The arterial walls were sclerotic. The right pupil was more dilated than the left, and both reacted to light and accommodation. The tongue was dry and coated, with a slight pyorrhea of the gums.

In the thorax the expansion was poor. The spine was tender to pressure over the upper dorsal region. The ribs and clavicles were prominent, with deep supra- and infraclavicular fossæ. Anteriorly, both apices were dull, with the breath sounds bronchial in character, fremitus increased, an occasional rale, bronchophony and pectoriloquy. The breath sounds elsewhere were harsh, with prolongation of expiration. Posteriorly, both apices were dull as far as the middle of the scapulæ. Over this area the breath sounds were harsh. At the left base upon deep inspiration there was a "cogwheel" breath synchronous with the pulse.

The blood-pressure was systolic 120 and diastolic 75. The heart sounds were of good quality and tone; the first apical sound was loud, the second valvular, the aortic and pulmonary, especially the latter, were accentuated.

As to the extremities the reflexes were increased. The left leg was extremely amaciated. The left thigh upon flexion was 1.5 cm. smaller than the right. Pain was present in the hip-joint upon motion.

The following notes were observed from day to day:

April 5. Urine analysis: no albumin, sugar or casts. Blood: hemoglobin, 74 per cent.; red blood cells, 4,700,000; white blood cells, 8000; polynuclears, 70 per cent.; lymphocytes, 28 per cent.; large mononuclears, 2 per cent. The feces were streaked with blood and mucus.

April 6. The pupils were equal today. The sputum was negative for tubercle bacillus.

April 7. It was noted by Dr. Stengel that the right pupil was dilated; dulness to percussion was distinct anteriorly and posteriorly on the left.

April 8. Urine analysis: no sugar; a trace of albumin with light and dark granular and hyaline casts. A second specimen of sputum was negative for tubercle bacilli. Occult blood was positive in the feces, with a faint trace of bile. Dr. Grayson noted upon laryngeal examination that the right vocal cord was free while the left was fixed and immobile. A rectal examination was negative.

April 9. The Wassermann was negative. The patient complained of pain along the right costal border, with tenderness upon palpation over the ascending colon. A cutaneous nodule in the abdominal wall is noted as increasing in size.

April 11. The examination of the eye-grounds was negative. The stomach was noted below the umbilicus. A test meal resulted as follows: total acidity, 40 per cent.; free hydrochloric acid, 18 per cent. lactic acid negative, faint trace of occult blood.

April 14. Von Pirquet was faintly positive. Upon roentgen-ray examination the stomach seemed pushed to the left, with the shadow of a large mass, taken to be the liver, to the right, indicating a possible involvement of the right and left lobes.

April 15. The nodules in the skin and liver were increasing in size.

April. 16 A roentgen-ray examination of the chest by fluoroscope showed a shadow at the left apex suggesting either fluid or a solid growth into the lung.

April 18. Dr. Stengel noted no localized area of fluid at the left apex. The percussion note was dull posteriorly on the left, extending down below the angle of the scapula, and was becoming more marked. Auscultation anteriorly revealed breath sounds bronchial; posteriorly fremitus diminished, breath sounds distant, and tubular with bronchophony.

April 19. The patient was seen by Dr. Martin, who suggested a probable secondary carcinoma of the liver, lung, and spinal cord, with the primary focus in the sigmoid or cecum.

April 21. Ptosis of the left eyelid was marked. The blood showed hemoglobin, 27 per cent.; red blood cells, 3,300,000; white blood cells, 4000.

April 23. The abdominal nodule was removed.

April 25. The glands were noted enlarging on both sides of the neck.

April 27. Microscopic report on the nodule was made by Dr. Speese. The majority of the cells, cylindrical in shape, are infiltrating a stroma, suggesting sarcoma, but their type resembles carcinoma of glandular origin.

April 28. The patient had three convulsions of the entire body, Jacksonian in type. The right side of the face was involved, the tongue protruded to the right, next both upper extremities and body, and finally both legs, especially the right. During the convulsions the body was blue, afterward became red, followed by right-sided unilateral sweating. A spinal puncture was made at this time; the pressure was 40 mm.; the fluid dropped 140 times per minute. The blood-pressure now was systolic 140 and diastolic 75 on the right side, systolic 130 and diastolic 85 on the left side. During the attack the patient was unconscious, with a heart rate of 145.

April 19. Patient was unconscious and now had a right-sided hemiplegia. The blood-pressure was systolic 115 and diastolic 60. A spinal puncture resulted in no fluid. The eye-grounds were negative.

April 30. The patient died. The temperature was normal or subnormal, and never higher than 99° until this morning, when it went up to 100°, and just before death to 100⅘°. The respirations ranged between 20 and 25 until April 28, when they went up to 28 and on up until at death they were 40. The pulse averaged 110 until April 28, when it went up to 160, corresponding to the rise in temperature.

Autopsy Protocol. J. M., 4485, 14–89, died April 30, 1914. The autopsy was made at the University Hospital a few hours after death. The body is that of an adult white male about fifty years of age. General amaciation is marked, not unlike that of the pictures of cholera patients without the septic facies. The pupils are slightly dilated and equal. The conjunctivæ are cloudy, especially at the angles. The teeth are still present in fair shape, with considerable sordes, and the mucous membranes are pallid.

A tumor mass is palpable on the right radius midway between the elbow and the wrist. Upon preliminary incision the abdominal wall is less than one-half inch in thickness; the adipose tissue has entirely disappeared. The musculature is dark and greatly atrophied.

In the abdomen the liver extends four fingers' breath below the costal margin. On its under surface there is a firm inflammatory adhesion which extends to the white line of the transverse colon at the hepatic flexure. This has produced a distinct constriction. Fom here the transverse colon has a well-marked midline ptosis, the angle being down in the pelvis. Beyond this the transverse colon becomes smaller (up to this point it has been dilated) and the entire descending colon is small and contracted. The small intestine is contracted, and much of it puddles in the pelvis. The cardia of the stomach extends well down; near the pylorus it makes a sharp kink to the right, the pylorus thus coming to lie below the head of the pancreas, crossing the transverse portion of the duodenum, causing the first and second portions to be greatly distended.

The liver (Fig. 2) weighs 2400 gms., and measures 27 x 22 x 9 cms., the organ is generally pallid, with blotchy areas of blue. On the surfaces, both the superior and inferior, especially of the right lobe, there are seen numerous raised white masses, sharply defined and varying in size from 5 mm. to 4 cm. Some of these masses have central depressions with radiations toward the periphery. Upon cut section the masses are seen to extend throughout the liver structure, one large one being 6 cms. in diameter. These masses have central necrotic areas which are soft and drip away on section. The liver structure is pallid, lobular markings very poorly defined. The gall-bladder is small, contracted, and not in any way connected with the tumor mass. It contains about 5 c.c. of a dark viscid bile. Bile ducts are patulous.

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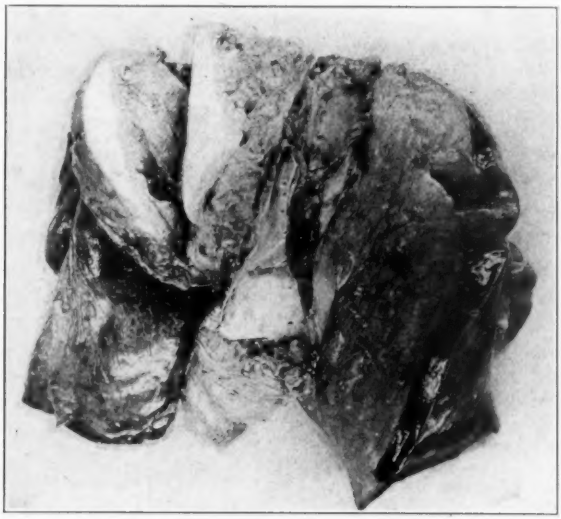

FIG. 1.—A posterior view of both lungs, heart, tumor, and aorta. The tumor is one large mass occupying the apex and posterior portion of the left lung. (Original.)

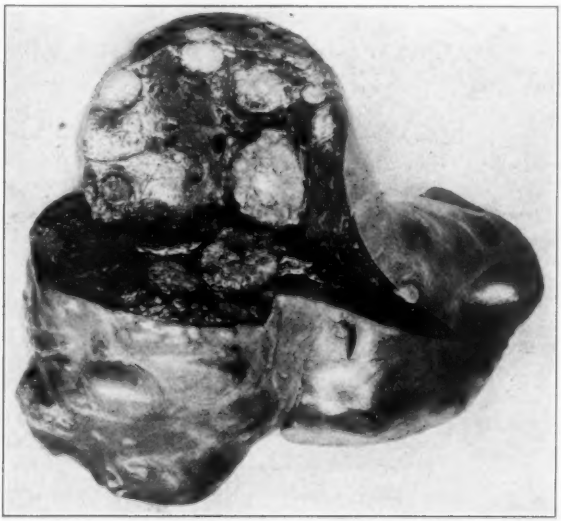

FIG. 2.—The liver is studded with nodules of various sizes showing all the characteristics of metastatic tumors. (Original.)

The stomach contains several hundred cubic centimeters of a greenish, liquid content. The stomach wall is thin, the vessels injected with blue blood. On opening it the rugæ are easily flattened out. There is present an excess of mucus with a general submucosal injection.

The walls of the small intestines are thin; submucosal injection is moderate. The lower part of the ileum contains hard fecal masses, and in this part the mucosa becomes dark and blue.

The pancreas measures 21 cms. in length and is correspondingly broad and thick. The organ is pale yellow. Upon section the lobules are fairly definite, and there is a good deal of bright yellow color to them.

The left adrenal is small and firm, and has a very little fat about it. On section it shows a dark medulla and a yellow cortex.

A small retroperitoneal lymph node lies in close relation but is not adherent to it.

The left kidney weighs 220 gms., measures 13 x 5 x 4.5 cms.; the organ is firm, pale blue, cuts with ease, and the cut edge bulges. The capsule strips without much difficulty; is adherent but does not tear. Upon section the surface is blue, especially so at the upper portions of the pyramids. The darker portion of the latter has considerable fibrous tissue, which sends parallel interlineations into the cortex. There is a fine granularity to the cortex upon reflected light.

The right adrenal resembles its fellow on the opposite side.

The right kidney weighs 210 gms., and measures 13 x 6 x 3 cms.; the organ resembles its fellow on the opposite side, except that it shows more of the blue color. Upon section of this kidney there is one small mass, 2 mm. in diameter, which upon section looks like a secondary tumor mass.

The urinary bladder contains 50 c.c. of a light amber urine. The bladder wall is thin.

The spleen weighs 125 gms., and measures 11 x 6.5 x 3.5 cms.; the organ is soft. The capsule is wrinkled and shows no secondary involvement; cuts with ease; the splenic pulp is mushy; trabeculæ and follicles are not prominent.

The pleural cavities are free from fluid and show a few adhesions at the base on the right side. The left apical portion of the pleura (Fig. 1) contains a mass measuring 14 cms. in length and 11 cms. in thickness. This is a pale mass of tumor material which has apparently sprung from the pleura and is growing downward over the upper lobe and between the pleural surfaces of the upper and lower lobes of this lung. Toward the midline it surrounds the arch of the aorta for a distance of 10 cm., and this is constricted so that one finger is admitted with difficulty into the lumen. Posteriorly the tumor erodes the vertebræ, so that it is possible to place the index finger into the spinal canal. The third rib at its union with the vertebra is eroded and fractured. Many of the mediastinal lymph nodes are enlarged, some the size of a large walnut; one large one

lies in close relationship to the trachea, the lumen of which it has narrowed.

The left lung has a dark bluish color, more blue in the dependant portion, and has a boggy feel. Upon section, frothy blood-tinged fluid exudes. Just beneath the tumor in the upper portion of the lower lobe there is a triangular raised area, which upon section is dark and granular, presenting a line of lighter demarcation.

The heart was removed in the mass with both lungs and the tumor. The pericardium contains 50 c.c. of a clear serous fluid. The heart is small, rather distinctly bronzed, with remnants of the subepicardial fat along the coronaries and the septæ. The coronary

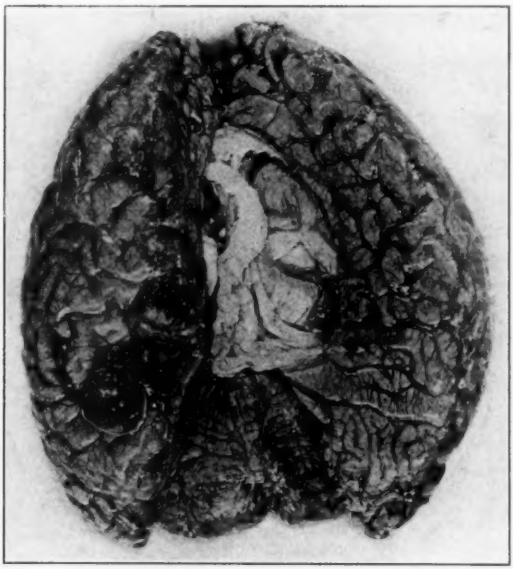

FIG. 3.—The brain presents a small nodule on the convex surface of the left cerebrum just behind the paracentral lobule. (Original.)

vessels are engorged and blue. The epicardium shows numerous white lines of thickening. The left ventricular wall measures 1 cm. The musculature is pallid and soft, and there are streaks of yellow here and there. The aortic valvular orifice measures 7 cm.; valve leaflets are thin, with some adhesions at the angles. The mitral orifice measures 9 cm.; valve leaflets are thin except at the attachment of the chordæ tendinæ. The latter are thin and lengthened out and the papillary muscles short and thin. The right ventricular wall measures 3 mm. and the tricuspid orifice 14 cm.; the leaflets are thin. The pulmonary orifice measures 7 cm.; the leaflets are thin.

The aorta has lost its elasticity; there is some thickening in a wavy fashion to the intimal surface. The constriction noted above is in the descending arch just beyond where the vessels pass off.

In the brain (Fig. 3) the dura over the middle portion of the upper surface of the left hemisphere in the midline is adherent to a mass 3 cm. in diameter, which has evidently arisen from the dura, pushing the brain substance ahead of it. In this growth in the cerebrum the mass has undergone considerable softening.

The spinal cord shows no lesion grossly at the position of the erosion through the vertebral column. Apparently neither involvement of the spinal meninges nor of the cord is present.

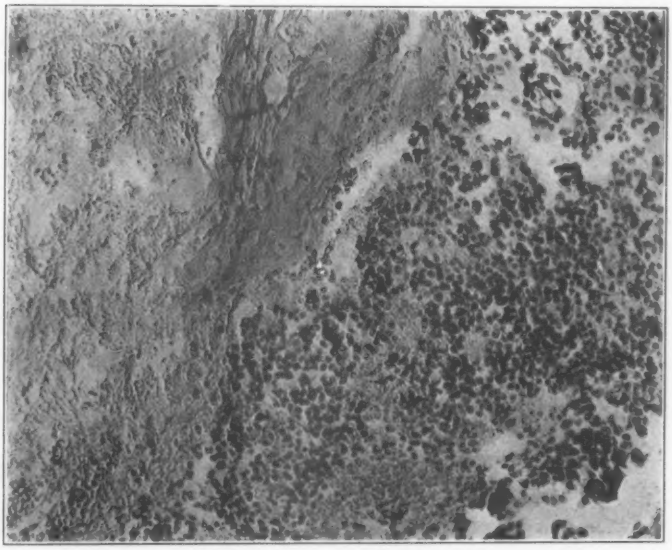

FIG. 4.—The section includes the tumor springing from the surface of the thickened pleura. A large endothelial type of cell occurring in masses with necrosis of central groups. (Photomicrograph, original.)

The following tissues were prepared and submitted for histological examination: lung, pleura, tumor and bronchus, peribronchial lymph node, heart, aorta, liver, spleen, pancreas, adrenals, kidney, stomach, mesenteric lymph node, and tumor of the forearm.

1. In a section of the lung taken from the dependant portion, hemorrhage, congestion and edema is very marked. There are no areas of necrosis in this, so that infarction is ruled out. An exudation of cells, mostly polynuclears and fibrin, is marked throughout the section. Collections of large endothelial cells of the phagocytic type, containing dark brown pigment of hemosiderin, are seen.

Another section from the lung shows a fibrous pleural surface, the

alveolar walls thin, spaces in places collapsed, in others widely dilated and rupturing into one another. There is a moderate anthracosis in this part of the lung. Here (Fig. 6) the spaces are filled with a small amount of exudative material, desquamated alveolar cells, some round cells, and large numbers of phagocytic cells containing hemosiderin. Some of the spaces have dense masses of tumor cells. A large bronchus, which is dilated, shows desquamation of its lining cells, and contains a moderate number of polynuclears and tumor cells. All of the vessels are congested, and some of the smaller ones have ruptured.

2. A section through the tumor mass (Fig. 4), including the pleura, shows a more active proliferation of the cells of the pleura than elsewhere, with extension of these cells along the alveolar walls, forming a new fibrous network. In a section of the pleura, including the tumor and aorta, the tumor is seen to be made up of a considerable growth of fibrous network, which is actively proliferating along with the tumor growth. This coarser network runs out into a finer fibrillar structure, leaving spaces which are filled up with tumor cells. There is one definite type of cell running through all the sections of the tumor. It is round, in places it is lengthened out and looks like a columnar cell. In other places it is flattened out and looks like a plasma cell; it has a moderate amount of acid-staining cytoplasm and a centrally placed nucleus dark and hyperchromatic or light and vesicular. Karyokinetic figures are not well seen. The cells in places group in masses, forming a syncitial type. Where they are round or similar to columnar epithelium they seem to be following the lines of embryonic vessels, so that the arrangement of hypernephroma is suggested. A mass of well-stained cells often lies in immediate juxtaposition to a group of cells which are necrotic. A moderate number of round cells of the lymphocytic type are intermingled with the tumor cells. In places the cells seem to line spaces as though they were trying to carry out their normal function. Where the tumor mass is close to the aorta it has infiltrated the adventitia and stopped at the median coat. This portion of the aorta shows a loss of the fibro-elastic tissue both in the intima and media, with replacement by a loose type of fibrous tissue. In the intima degenerative changes of a fatty nature have taken place.

3. In a section of tumor and a large bronchus (Fig. 5), one makes out the mucosal lining of epithelium in places thinned and desquamated. There has been a slight submucosal injection and fibrosis. The glands show a moderate catarrhal change, with the presence of goblet cells and mucin in their lumens. At the fibrous union of the cartilaginous rings the tumor cells are attempting to penetrate. If ulceration occurred at this point they might readily get through and continue to grow along the bronchus. Beyond the line of the cartilage the perichrondrium is somewhat thickened and the tumor mass may be seen growing against it—well defined, however, by the density of its tissue. The tumor has penetrated as far as it

can against the cartilage. The same type and grouping of the cells are seen, with the exception that there is not the extensive necrosis as seen in the primary tumor.

4. The peribronchial lymph node shows an increase in original fibrous tissue. The infiltration by the tumor is wide-spread throughout the node, especially the central part.

5. In the heart the epicardium is thin. The section has not included a milk plaque. The subepicardial fat is decreased. The coronary vessels are injected and show throughout some thickening of their walls. There is a very slight increase in the fibrous tissue of the intermuscular septæ. The cardiac muscle has lost a good deal

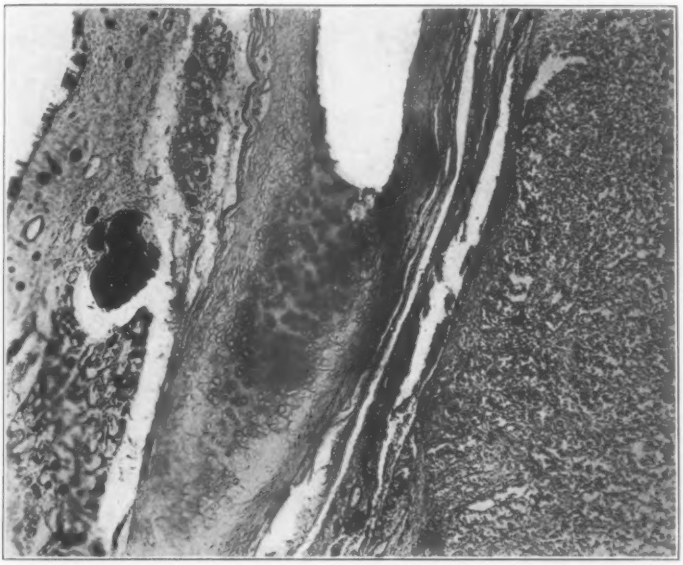

FIG. 5.—To the left of a cartilaginous ring of the trachea is the congested mucosa with swollen and desquamated epithelium; to the right the tumor has grown up to the perichondrium. (Photomicrograph, original.)

of its structure, the fibers being thin, pale staining, and fragmented; the striations are poorly defined; numerous small vacuoles are present, the nuclei are mostly small and pyknotic, and there is very little tendency to a deposition of myohemoglobin.

6. The aorta, taken from the abdominal portion, shows the changes described above in connection with the tumor. If there is really any change, fibrous replacement here is more marked and there is a general contraction of the coats, so that the width of the aorta is relatively less than usual.

7. In the liver there is a tendency for the structure to be open, due probably to fixation. Many of the red blood cells in the section have

been washed out, leaving the dilated vessel spaces. Congestion has been more marked about the central lobular veins than elsewhere. Here the liver cells are filled with the brown pigment of hemosiderin. These cells are small. The nuclei show clearly, the protoplasm is granular and pale staining, and contains multiple small clear-cut vacuoles. In the periphery of the lobules the condition of turbidity and granularity may be still made out, but the vacuolization is not as prominent. A third section was taken in connection with the tumor growth. In this the tumor is more or less sharply outlined—not so much by fibrous tissue as by a condensation of the liver cells. Here the cells are compressed closely together—they are small, filled

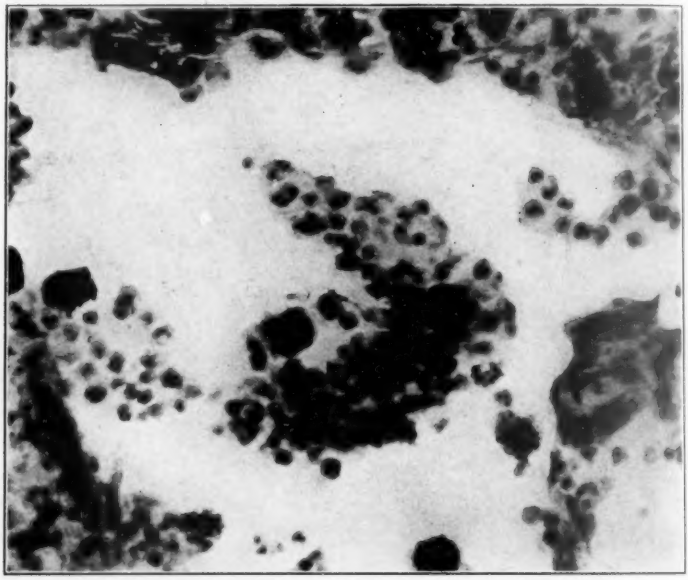

FIG. 6.—The contents from the alveolus of the lung, polynuclear, leukocytes, lymphocyte, phagocytic endothelial cells, and tumor cells. (Photomicrograph, original.)

up with a large amount of pigment, and many of them are vacuolated. The tumor in this situation takes on very strongly the characteristics of epithelial cells, the cells being attached by the base along the lines of fine embryonic bloodvessels. Their nuclei are very vesicular and karyokinesis is more often seen. In some places where these new bloodvessels have been cut transversely the cells are more of the plasma type. The same tendency to necrosis in the center of these masses is present, as in the parent growth.

8. The spleen shows the capsule slightly thickened, irregular and faint staining; the trabeculæ are not prominent. The Malpighian bodies are small and there is a tendency to hyalinization of the coats

of the central arterioles. In the general splenic structure there are a few pulp cells; congestion has been marked, many of the red blood cells appearing as ghost corpuscles. The deposition of a golden-brown pigment is excessive throughout the section.

9. In the pancreas, from the gross description, one might expect to find considerable fatty infiltration, but such is not the case. The lobules of the pancreas are widely separated from one another and the spaces are empty; presumably this was fluid. The general interstitial matrix is thin and fibrillar in character. This same looseness and edema is noticed in the lobules and between the individual acini. There is a tendency for the pancreatic cells to take the stain in different ways; some of these fail to take the stain at all, and may be due to fixative faults. These cells, however, are quite brown in color, suggesting the blood-staining of passive congestion. In the basic stain they appear small and compact, with the nucleus poorly defined and fragmented. The islands of Langerhans are loose and consist of few cells.

10. In the adrenals the capsule is thin; fibrous tissue trabeculæ are not excessive. The zones of the adrenal are well-marked and the cells take on different characteristics, so that one gets the appearance of openness throughout. Most of the cells are pale staining and show vacuolation described in the cortical susbtance. When the cells show protoplasm this is acid-stained and fragmented; the nucleus is small and pyknotic and the chromaphilic property of all the cells, even those which are very badly vacuolated, is very marked. This section suggests in its varied pathology that if the organs of internal secretion play any part in the tumor formation an example is here present.

11. The kidney shows the capsule thickened, loose and edematous, with a tendency to penetrate. Congestion of the cortex, moderately advanced, is present throughout. The glomerules show the spaces of Bowman dilated, capsules thickened, glomerular tufts decidedly thickened, compact, and containing many nuclei. The secreting tubules are distended, the individual cells are in a state of granularity, and have been flattened out against their basement membranes. In other words the tubular cells are small but show a marked grade of cloudy swelling. The protoplasm of the cells in places is badly fragmented and possibly vacuolated; some loss of protoplasm is evident in the collecting tubules. The fibrous tissue of the pyramids is not increased but the spaces are open and filled with edema. One of the glomerules seems to be filled up with a small clump of tumor cells—at least the cells correspond in character to those seen in the sections of tumor.

12. In the stomach the thinness of the wall as described grossly is quite apparent. This is due to a loss in the muscular coat and the openness due to fluid in the submucosal coat. There is a moderate injection of the submucosa and rather marked injection of the mucosa. The mucosal lining is separated from its submucosal

fibrous tissue. The epithelial cells of the mucosa show varying degrees of goblet formation, with the lumina filled up with acid-staining mucus.

13. The mesenteric lymph node shows the same tumor formation as characterized the peribronchial lymph node.

14. A section taken from the tumor in the forearm shows a bit of the voluntary muscle along one side, with the characteristic development of the tumor in the nodule. The same fibrous tisssue network, the same islands of cells, and the same necrosis as described elsewhere. In the brain a small mass imperfectly globular, protruding to the surface on the median side of the left hemisphere just behind the paracentral lobule, friable, is about the size of the end of the thumb. When a horizontal section is made through the hemisphere this mass is found entirely loose in the brain substance, where it lies in a cavity. It does not extend to the lateral ventricle. A piece contains a clot. Endotheliomatous cells in groups are found close to the clot.

The following diagnoses are made from the autopsy protocol: A primary endothelioma of the pleura with extension to the lung, metastases to the mediastinum, liver, kidney, lymph nodes, skin, right radius, and dura. The lungs: chronic fibrous pleuritis, passive congestion, hypostatic congestion edema and pneumonia, anthracosis, atrophy with atelectasis and compensatory emphysema. The heart: chronic fibrous epicarditis, chronic parenchymatous myocarditis with atrophy. The arteries: chronic fibrous panarteritis. The abdomen: chronic fibrous peritonitis (bands). The liver: passive congestion, chronic parenchymatous hepatitis, including cloudy swelling, fatty metamorphosis, and hematogenous pigmentation. The spleen: passive congestion with atrophy. The pancreas: atrophy with edema and parenchymatous degeneration. The kidney: passive congestion with chronic parenchymatous nephritis. The adrenals: chronic parenchymatous adrenalitis. The stomach: chronic atrophic catarrhal gastritis. The skeleton: erosion of the vertebræ and third rib with fracture of the latter and erosion of the radius.

In the correlation (Fig. 7) of this case one is quite able to study, with a considerable degree of satisfaction, the course of the disease. The duration was approximately one and a half years. Serious symptoms were present over a period of a year, with a progressing intensity. The primary growth gave the cardinal symptoms of lung involvement, cough, expectoration, and dyspnea. Terminally the objective signs are easily explained by the solid mass. The roentgen-ray shadow is interesting. The metastases developed their symptoms, especially the brain mass. The negative eye-grounds are explained by the size of the mass. The condition of the stomach might in itself explain the vomiting, but many such types are encountered at autopsy when vomiting was not present. The constipation is easily accounted for by the condition of the intestines if one looks

at it from the stand-point of intestinal stasis. This, too, may explain the early headache; the fixation of the left vocal cord by the involvement of the recurrent laryngeal nerve; unilateral sweating by the

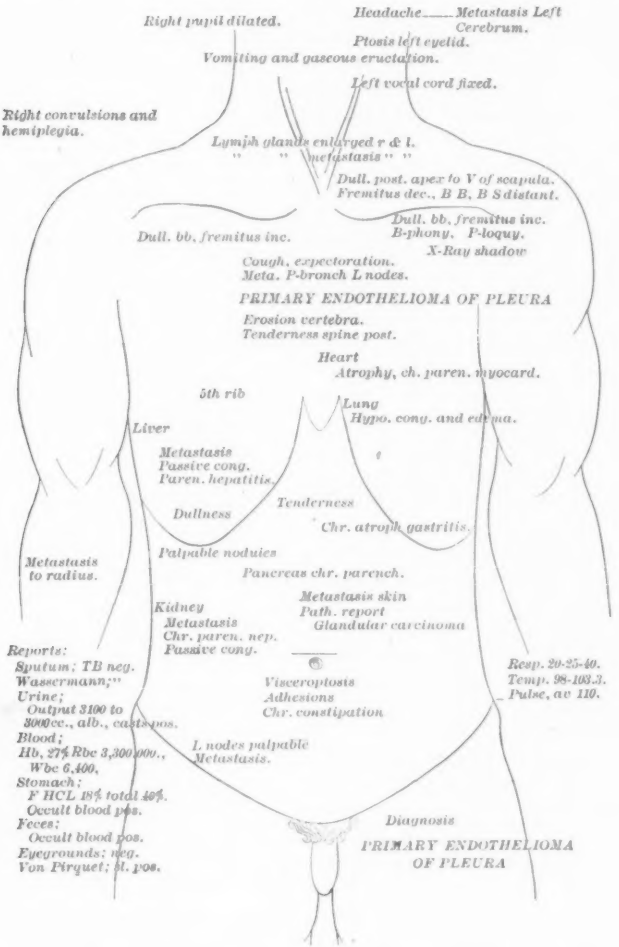

FIG. 7.—A graphic chart of the clinical signs, symptoms, and reports, with the corresponding autopsy findings. This method of presentation is specially useful for teaching purposes using lantern slides.

involvement of the sympathetics and the tenderness over the spinal region posteriorly by the erosion of the vertebræ and rib are readily explainable. The passive congestion was produced by the pressure

on the vena cava and the myocardial changes, while the pressure on the aorta resulted in a marked constriction. Under ordinary circumstances one would expect to find at least some evidence of a left-sided hypertrophy of the heart, and it may be said, I think correctly, that the factor nutrition lacking in this case not only did not permit an hypertrophy but actually was in part responsible for an atrophy. The presence of a mucopurulent sputum with a negative tubercle bacillus would seem to be especially significant.

From the pathological point of view we are dealing with a primary growth of considerable size, showing wide-spread yet slow multiple metastases. In studying these slides I cannot get away from the idea of an association of this tumor with a specific inflammation. The types of cells, their great individual variation, their groupings with a tendency to necrosis, marked evidences of simple inflammation, all lead me to one idea that this pathological complex has many of the features of a specific inflammation. The cells group themselves in places much like glandular epithelium; in these parts connective tissue is profuse. In other places large groups of cells collect in masses with almost no connective-tissue framework. Here often blood channels are made out of the cells and large areas are necrotic. The cells in the metastatic nodules are more characteristic of the endothelial type, but here the gross lesions very closely resemble carcinoma, as in the liver. On the other hand the brain nodule might have been a primary tumor arising from the dura.

From a study of the types of cells found in the bronchi I would suggest the possibility of making a tentative diagnosis clinically from the examination of the sputum.

Conclusions. 1. Primary endothelioma of the pleura is relatively rare and from the literature occurs as a single tumor or as multiple nodules. Progressive loss of weight, dyspnea, and fluid in the chest are the most common symptoms. The tumor shows an endothelial type of cell with epithelial groupings hence, often, the name endothelial cancer.

2. Clinically this case was of seventeen months' duration. The patient presented loss of weight, weakness, cough, expectoration, headache, vomiting, gastro-intestinal symptoms, chest signs of consolidation, roentgen-ray shadow over the primary growth, metastases, palpable lymph nodes, palpable liver with nodules, fixation of the vocal cords, negative sputum and Wassermann, and secondary anemia. The case terminated in a nephritis, cardiac failure, Jacksonian convulsions, and hemiplegia.

3. Pathologically there was one large primary mass arising from the pleura, composed of endothelial cells in various types and arrangements, with extension to the lung, bronchial lymph nodes, trachea and bronchi, and compression of the aorta. Metastases followed to the liver, kidney, lymph nodes, abdominal skin, right radius and brain, with erosion of the spinal bony column and fracture of a rib.

REVIEWS

A Manual of Pharmacology, Adapted to the 1916 U. S. Pharmacopœia, and its Applications to Therapeutics and Toxicology. By Torald Sollmann, M.D., Professor of Pharmacology and Materia Medica, Western Reserve University, Cleveland, Ohio. Pp. 901; illustrated. Philadelphia and London; W. B. Saunders Company, 1917.

This volume, the product of a careful compilation of innumerable references and facts established clinically and experimentally, affords an excellent source for either reference or study. It is, indeed, an ambitious undertaking and one commensurate with the extensive development of theoretical and practical pharmacology. A great mass of minute details are presented, far too great, in fact, to memorize; but their presentation is clear and concise and where points are still in dispute, recent studies by various workers are briefly offered, the decision of the correct interpretation of the points at issue frequently being left to the reader. The references, especially to the recent literature, are well selected and numerous, as is revealed by an unusually extensive bibliography at the end of the book.

As the author states in the preface, it has been his purpose to present, without confusion, the broad conceptions and generalizations, as well as the detailed conclusions comprised in pharmacology. With this end in view, the nature of the book is as follows—large print is interspersed with small, the former giving a connected and concise statement of the essentials of pharmacology as offered by any good text-book on the subject, while the latter, *i. e.*, the small print, contains more detailed data for consultation and is replete with references to the literature. The liberal use of side headings is a distinct advantage.

In revising the text-book of pharmacology, the enlargement required the separation of the laboratory guide in pharmacology which has appeared as a companion volume. This separation offers several advantages at once apparent to the reader. The discussion of the many drugs of slight importance has been curtailed, more space thus being left for the fewer drugs of greater value.

There are no numbered chapters in the book, the first part of which is allotted to the elementary principles of pharmacology,

following which a general discussion of the treatment of disease is offered. Next the various drugs in their respective groups are considered, the space allotted to each being governed by the importance of the drugs discussed. Aside from those arranged in groups, a great many other drugs of minor import are briefly described. Certain portions of the text of the United States Pharmacpœia are inserted. At the back of the book will be found an appendix presenting a tabulation of average doses, a check list for the study of preparations and an extensive bibliography.

This volume has a large sphere of usefulness not only as a text-book, but also as a reference to the pharmacological literature.

A. H. H.

THE INTERNATIONAL MEDICAL ANNUAL, 1916. Pp. 735; 66 illustrations. New York: William Wood & Co.

IT would seem that too much has been attempted for a book of this size. To attempt to mass together the important literature of a year on all branches of medicine is, of course, an enormous undertaking. Certain subjects are considerably slighted, notably pediatrics. The war has greatly diminished the output of ordinary European medical work, although it has resulted in much writing on war surgery. This is thoroughly covered in the *Annual*. The reviewer believes that if books of this type are used at all they should be separate volumes on definite specialties. A. G. M.

A LABORATORY GUIDE IN PHARMACOLOGY, ADAPTED TO THE 1916 U. S. PHARMACOPŒIA. By TORALD SOLLMANN, M.D., Professor of Pharmacology and Materia Medica, Western Reserve University, Cleveland, Ohio. Pp. 355, illustrated. Philadelphia and London: W. B. Saunders Company, 1917.

THIS book, a companion volume of the author's *Manual of Pharmacology*, has for its purpose the familiarization of the student with the more important facts of pharmacology by way of observations obtained at first hand in the laboratory. The volume is divided into two parts. Part I is devoted to the essential features necessary to the medical student and includes a series of pharmaceutic and toxicologic exercises arranged for a course of thirty working periods of two to three hours. Part II consists of a series of experiments on animals, affording a direct means for the student to observe the pharmacologic action of the more important drugs.

The problems of impaired functions are thus introduced and their correction by therapeutic agents suggested.

Additional optional experiments are offered. The arrangement of the exercises throughout is clear cut and concise. Introductory remarks, explanatory notes, numerous illustrations and diagrams add to the value of the book to the student. For the instructor, several features contribute to its usefulness, among which may be mentioned the systematic arrangement throughout, the technical references and the contents of the appendix at the end of the book.

A. H. H.

THE HEALTHY GIRL. By MRS. JOSEPH CUNNING, M.D., and A. CAMPBELL, B.A. Pp. 190; 23 illustrations. London: Oxford University Press.

THE attempt of the authors is laudable, "To help the girl who is leaving school and learning to face life, to understand the most important circumstance she is likely to encounter herself." To a certain extent a growing girl might read this book with profit, although it is written in a manner which would be more capable of interpretation and benefit to mothers and teachers.

Elementary anatomy and physiology are entered into, in order to explain the nervous system and digestion; as well as the bad effects of posture and lack of exercise. There are chapters on Work and Rest; Fresh Air and Breathing; Bad Habits; The Open-air School and Menstruation. In the chapter on Teeth the authors go a little too far, or rather are perhaps not sufficiently discursive, when they leave the impression that all osteo-arthritis, gout, neuritis, etc., are due to pyorrhea and decayed teeth. The statement is made that neurasthenia is due many times to unhealthy condition of the gums and teeth. The reviewer is of the opinion that in a book ostensibly written for the lay public, it would be better not to make statements such as the above, unless they are qualified.

Altogether the book is readable, although not remarkable, and may serve a useful purpose.

A. G. M.

MODERN METHODS OF TREATING FRACTURES. By ERNEST W. HEY, the Bristol General Hospital, etc. Pp. 286. New York: William Wood & Co.

THE interesting introductory chapter entitled the Myths of Yesterday and the Problems of Today deals with general considerations of fracture treatment and emphasizes the disadvantages of

treatment by immobilization alone as formerly practised, and states that the modern problem is to secure perfect joint action and to preserve the full vitality of the circulation and neuromuscular apparatus. The keynote of the book is the author's aim to show that as occasion requires there should be brought into service the newer methods: (1) massage and mobilization, (2) extension methods, and (3) operative methods rather than to regard them as rival systems. His method of double transfixion offers a distinct advance in extension treatment. An excellent chapter on operative treatment is based upon experimental work done by the author with the assistance of grants made by the Science Committee of the British Medical Association. After describing the technic of operative treatment as applied to patients he deals with certain special fractures, with due attention to mechanical accuracy and efficiency.

The illustrations of the results of experimental work are especially commendable. The book is written in precise style and with convincing clearness. It is worthy of careful reading by experienced surgeons, since it is indeed "modern," and is based upon a large amount of clinical and experimental study. G. M. L.

CANDY MEDICATION. By BERNARD FANTUS, Professor of Pharmacology and Therapeutics, College of Medicine, University of Illinois. St. Louis: C. V. Mosby Company.

THOSE who are called upon to treat children often encounter the child who refuses medication. Again, some drugs are obnoxious to any child. Dr. Fantus tells us how to give many drugs (indeed, many more than most of us will use) in an attractive and palatable manner. The method of preparation and dispensing as described is not difficult, and is well worth while knowing. The book contains a rather elaborate formulary. A. G. M.

A MANUAL OF SURGICAL ANESTHESIA. By H. BELLAMY GARDNER, Honorary Anesthetist of the King George Hospital, etc. Second edition. New York: William Wood & Co.

THE author has in part rewritten this book for the second edition and has added several new chapters. He gives a history of anesthesia, a chapter on cardinal principles in which he emphasizes the importance of avoiding anaxemia and properly makes this the keynote of the entire volume. In subsequent chapters the phenomena of anesthesia are fully described and considered from the standpoint

of physiology so that the method employed may be selected with reference to the type and temperament as well as the pathologic condition of the patient. He gives an adequate description of the more important general anesthetics and the apparatus for their administration. The chapter on spinal anesthesia is too brief to be of much value. There are many useful hints for dealing with certain special operations. The volume is fairly well illustrated and is printed in large type. It is written for the student and practitioner and is especially to be recommended to dentists, since the author has paid particular attention to the technic of anesthesia for dental operations. One could take exception to the practice of touching the cornea to observe the corneal reflex as being unnecessary and dangerous. The work is essentially a practical treatise based on accurate observation and large experience. G. M. L.

EPIDEMICS RESULTING FROM WARS. By DR. FRIEDRICH PRINZING. Edited by HARALD WESTERGAARD, Professor of Political Science in the University of Copenhagen; Member of the Committee of Research of the Division of Economics and History of the Carnegie Endowment for International Peace. Pp. 346. Oxford: At the Clarendon Press, Humphrey Milford.

THE stated purpose of the Division of Economics and History of the Carnegie Endowment for International Peace is to "promote a thorough and scientific investigation of the causes and results of war." Its members consist of statesmen, publicists, and economists. At a conference of this division in Berne, Switzerland, in 1911, thirty-seven questions and problems were drafted for extensive investigation, and it is stated that these are to be "discussed scientifically, and, as far as possible, without prejudice either for or against war." It is not obligatory that the members of this division shall make these investigations themselves, but that they shall select competent collaborators who shall present reports in the form of books or monographs. These reports must be read and edited by a member of the division, and are published upon his recommendation.

The monograph under review treats of the results of war from a point of view that is quite interesting to medical men and one that has not been sufficiently emphasized before. It shows that until recent times the greatest cost of life in war has not been from fatalities in battle or from disease among the soldiers, but from epidemics among the civil population. Emphasis is placed upon the epidemics associated with the Thirty Years' war and their important part in Germany's prostration afterward, the deaths from typhoid, smallpox, and dysentery in our civil war, the smallpox

epidemic following the Franco-German war, and the death rate in besieged cities, as Paris, where it was in 1870–1871 three times normal, and Port Arthur. Until comparatively recent times the plague and typhus were the most common of the pestilences of war, although cholera, dysentery, typhoid fever, and smallpox have contributed largely to many mortality lists.

The work is scientific, good reading, quite interesting historically, and is the statement of another point against war. T. G. M.

NERVE INJURIES AND SHOCK. By CAPTAIN WILFRED HARRIS, R.A.M.C., Physician to St. Mary's Hospital, London. Pp. 127. London: Oxford Med. Press.

THIS book is written for the physician, rather than for the surgeon. It is of particular value to him who has to deal with cases of nervous exhaustion, neurasthenia and functional paralysis of various kinds. G. M. L.

SURGERY OF THE HEAD. By MAJOR L. BATHE RAWLING, R.A.M.C., Surgeon and Senior Demonstrator of Operative Surgery, St. Bartholomew's Hospital, London. Pp. 150; 31 illustrations. London: Oxford Med. Press.

THE subject of head injuries is covered in a clear and practical description of applied anatomy, symptomatology of the various traumatic lesions, and the generally approved methods of treatment. The chapter on operative technic could have been amplified with advantage. Present-day warfare demands particular attention to the surgery of the jaws and orbit, and the author could have described more fully some of the work that is being done in this field with brilliant results. G. M. L.

MALAY POISONS AND CHARM CURES. By JOHN D. GIMLETTE, M.R.C.S., L.R.C.P., Residency Surgeon of Kelantau, One and Protected, Malay States. Pp. viii, 127. London: J. & A. Churchill.

THIS little book is a materia medica of the remedies and destructive poisons employed by the native "medicine men" of Malay and particularly of Kelantau. With his descriptions of the various medicaments and charms the author has given the local superstitions and translations of some of the native incantations. J. H. A.

INDEX OF 458 POSTMORTEMS OF THE INSANE. NUMBER 1181 TO 1638. By CHARLES J. SWALM, M.D., and ABRAHAM L. MANN, M.D. Volume II.

THIS is the second volume of indexes of the autopsies of the insane in the State Hospital for the Insane at Norristown. It is interesting as a statistical study of brains and some spinal cords in the various types of insanity. In Part II there is a valuable index of different brains in the various types of insanity and a classification of anatomical lesions other than those found in the brain and spinal cord. T. H. W.

NOTES ON THE CAUSATION OF CANCER. By the HON. ROLLO RUSSELL. With a preface by Dr. DAWTREY DREWITT. Pp. 116. London: Longmans, Green & Co.

THIS book, published by the author's wife and issued posthumously, is a continuation of Mr. Russell's statistical studies, particularly in the direction of food consumption, a subject in which he shows a strong leaning to vegetarianism. He starts out with a premise that there is no single cause of cancer but that irritation and injury are the causes. The injury may be mechanical or toxic, and he lays great stress upon local injury, as in pipe-smoker's lip cancer or tar-worker's skin tumors. The burden of this work, however, is to show that the principal causes of cancer are alcohol, tea, coffee, excessive eating, condiments, sour food (vinegar, wines, and cider), very hot food and drink, putrefying food, and, last and least, parasites.

The arguments supporting the contentions are stated flatly and without submitting them to a critical analysis, although there is a considerable show of seeming analysis. The book is not a great addition to the literature of neoplasms, as the methods used are perilously near those of the unreasoning protagonist. H. F.

MODES OF RESEARCH IN GENETICS. By RAYMOND PEARL, The Maine Agricultural Experiment Station. Pp. 182. New York: Macmillan Company.

IN this little book of five chapters is reprinted material which the author has brought together from a number of sources to meet the needs of those who have found merit in the original presentation and desire to make use of the methods and conclusions in their teaching. The subjects thus considered are the current modes of research in

genetics, biometric ideas and methods in biology, nature of statistical knowledge, problems of inbreeding, genetics and breeding. The compilation is timely and would be very useful to any one concerned in the study of any biological problem where statistical methods are used. Rarely would the medical man find application for the methods elaborated, but many conclusions have their significance for him. McC.

PSYCHOLOGY AND MENTAL DISEASES. A HAND-BOOK OF PSYCHOLOGY AND MENTAL DISEASES. By C. B. BURR, M.D., Medical Director of Oak Grove Hospital (Flint, Michigan) for Mental and Nervous Diseases. Fourth edition, revised and enlarged, with illustrations. Philadelphia and London: F. A. Davis Company.

IN this small volume the author has approached the subject of mental diseases by the psychological route. It is a revised edition and is intended as a primer for attendants and nurses insofar it should serve its purpose. The chapters on nursing and handling of mental cases are excellent. S. L.

CHILDREN. THEIR CARE AND MANAGEMENT. By E. M. BROCKBANK, M.D. F.R.C.P., Honorary Physician Royal Infirmary, Manchester. Pp. 259. London: Henry Frowde, Hodder & Stoughton.

THE work belongs to the category of "books for the mother" in which the attempt is made to instruct in the rudiments of nursery hygiene and dietetics.

The author wisely lays little emphasis on disease, but restricts himself largely to a consideration of the needs of the average normal child. Important as is an appreciation of the danger signals of illness, the note of alarm can be struck so loudly as to cause infinite worry to the mother and consequent harm to the child.

In the present volume the instruction is well within the limits of lay comprehension, sensible and reasonably safe from criticism. That all the statements and advice would meet with unqualified approval is, of course, more than could be expected. For the mother who is thrown on her own resources, such a book will prove of real help, but no book can take the place of experience or of advice and actual demonstration by a competent physician or nurse. A. G. M.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF
W. S. THAYER, M.D.,
PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,
AND
ROGER S. MORRIS, M.D.,
FREDERICK FORCHHEIMER PROFESSOR OF MEDICINE IN THE UNIVERSITY OF CINCINNATI, CINCINNATI, OHIO.

The Retinitis of Arteriosclerosis, and its Relation to Renal Retinitis and to Cerebral Vascular Disease.—R. FOSTER MOORE (*Quart. Jour. Med.*, x, p. 29, 37–38) reports his studies upon the retinal findings in 44 patients admitted to St. Bartholomew's Hospital suffering from cerebral vascular disease, and 66 cases which came to the Moorfield's Eye Hospital complaining of visual disturbances. The patients from St. Bartholomew's have not been traced, as they were already the subjects of cerebral disease, but 59 of the 66 patients seen at the Moorfield's Eye Hospital have been followed carefully for the development of cerebral vascular lesions. His observations, carried out in minute detail, lead him to recognize three varieties of retinal disease, all of which may occur in the same patient, but which usually appear separately, and have very different prognostic values. These three types of retinal disease are: (1) Retinal arteriosclerosis, in which the vessels of the retina appear tortuous, irregular in the size of their lumina, with obstruction of the blood flow in the veins where they are crossed by arteries, and other signs not so important. Hemorrhages also occur frequently in the retina. (2) Arteriosclerotic retinitis, in which the evidences of retinal arteriosclerosis are present usually in an advanced state, but in which are added exudates into the retina, which appear as small white dots usually scanty in number and often affecting only one eye (45 per cent. of the 31 cases). This is really an advanced degree of retinal arteriosclerlsis. (3) Renal retinitis, in which the arteriosclerotic changes are slight or absent, and large white patches of exudate, with edema and not infrequently detachment of the retina, are

observed. This is the type seen most frequently in chronic parenchymatous nephritis. In the chronic interstitial types the patches of exudate are smaller, the star figure about the macula is more frequent and hemorrhages in the retina are more extensive, while the arteriosclerotic changes in the retina are more marked. The author believes that in renal retinitis there is a toxic element added to the arterial cause of the retinal disease. The large white patches or "cotton-wool spots" seen in this affection never appear in arteriosclerotic retinitis. After a careful analysis of the 110 cases the author concludes that in the group of cases, 35 in number, showing only retinal arteriosclerosis, the mortality is lower, the incidence of gross cerebral vascular disease is less, and the blood-pressure is lower than in the cases, 31 in number, showing the changes characteristic of arteriosclerotic retinitis. Of the 44 cases admitted to the hospital suffering with gross cerebral vascular lesions 30 per cent. had no changes in the retinæ, 27 per cent. showed the changes of retinal arteriosclerosis and 43 per cent. had the characteristic retinal picture of arteriosclerotic retinitis. Thus 70 per cent. of the cases showed changes in the retinal vessels. Following up the cases from the Moorfield's Eye Hospital 27 are known to have died and the cause of death was ascertained in 26, 12 or 46 per cent. of the deaths resulting from a gross vascular cerebral lesion. Forty-six patients from the 66 included in his cases have been followed, and 21 or 46 per cent. are known to have developed gross cerebral lesions. Eighteen of the remainder are still alive so that the above proportion will be added to as time passes. The patients with arteriosclerotic retinitis live longer than the average patient showing renal retinitis, and, as can be seen, the percentage of deaths from cerebral vascular disease is much greater than that in renal retinitis, in which the average death is from "uremia" within about two years. Therefore the author feels that there is a form of retinitis which is associated with severe general arteriosclerosis, is secondary to local retinal vascular disease, and may be only incidentally associated with disease of the kidney, its ophthalmoscopic character, its significance and its prognostic value being largely distinct from the corresponding features of renal retinitis. The cause of death is referable to disease of the vascular system and not of the kidney, and the patients usually live somewhat longer than those suffering from so-called renal retinitis.

Intestinal Protozoa in Salonica War Area.—Lieutenant W. ROCHE, in his report to the Medical Research Committee (*Lancet*, 1917, excii, 297) gives the results of 1425 examinations of the stools of 893 cases of diarrhea and dysentery occurring among the troops of the Salonica war area. These cases occurred during the months of August, September and October, 1916, and the author makes the observation that the incidence of diarrhea and dysentery is proportional to the number of flies, decreasing during cold weather and very hot, dry weather during which times the flies are also diminished greatly, and increasing again as the flies increase in warm, moist weather. In the 893 cases nonpathogenic amebæ were found in 81 cases, and amebæ which were not identified because of lack of time in 39 cases. Entameba histolytica was found in 37 cases; Emtameba minuta in 47 cases. Flagellate protozoa were found in 217 cases divided as follows: Lamblia intesti-

nalis, 73; Tetramitus mesnili, 90; Trichomonas, 45; Cercomonas, 9. Coccidia were found in 18 cases. The author states that the bacillary dysenteries were predominant types, and observes that the comparatively few cases of acute amebic dysentery were interesting in view of the fact that many of the troops present in the Salonika area had been either in Egypt or Gallipoli and were Entameba histolytica carriers. The amebic cases were treated with 1 grain of emetin administered hypodermically every day for twelve days. The coccidia usually disappeared from the stools in a few days, but the lamblia and tetramitus infections were the most difficult to get rid of. Calomel, bismuth, salol, turpentine, thymol, emetin and Dale's double emetin were given by mouth with no result, and rectal irrigations with quinin, turpentin and eusol were also without effect.

SURGERY

UNDER THE CHARGE OF

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The Practical Application of the Wassermann Test in the Diagnosis and Control of Treatment of Syphilis.—CRAIG (*Am. Jour. Syph.*, January, 1917,.p. 192) says that the figures here given and the conclusions arrived at are based upon the results of 35,000 Wassermann tests personally performed and that the same technic has been employed in making all of these tests with the exception that, during the past two years, cholesterinized antigens have been used as well as antigens prepared from syphilitic fetal livers. As a result of his studies of these cases in the army the following deductions are made concerning the interpretations of the results of the Wassermann test: If the diseases, other than syphilis, that sometimes have given a positive result with the Wassermann test, can be excluded, a double-plus (four-plus of some writers) reaction is diagnostic of syphilis. Under such conditions, Craig considers this type of reaction as absolutely specific, whether symptoms are present or not, or whether there is or is not a history of infection. Under the same conditions, a plus reaction (three-plus or two-plus of some writers) may, in primary, tertiary, and latent infections be regarded as diagnostic, provided there is a clear history of infection, or suspicious clinical symptoms are present. In the absence of either history or clinical symptoms a plus reaction should not be regarded as diagnostic of the disease. A diagnosis of syphilis should never be made upon a plus-minus reaction. Many perfectly normal individuals give this type of reaction and it is of no value in the diagnosis of the disease except that it should be considered as negative. A single negative reaction, where there is no history of infection and where symptoms are not present, is of considerable value as a corrob-

orative sign of the absence of syphilis, but where there is any suspicion that the disease may be present it has very little value in excluding syphilis. It is only when a negative reaction is repeatedly obtained over a long period of time that it can be considered as good evidence of the absence of syphilis, and even then the spinal fluid should be tested and a provocative Wassermann test should be made after the reaction has remained negative for at least a year without treatment, and if this is negative, the spinal fluid should be tested.

The Advantage of Pyelotomy Drainage for Nephrotomy Wounds.—KEYES (*Jour. Urol.*, 1917, i, 91) says that a tradition has been handed down from the early days of kidney surgery warning us that incisions of the kidney pelvis heal badly. This tradition doubtless had its origin in the slow healing or permanent fistulæ resulting from simple drainage of the widely distended pelvis of a hydronephrotic kidney. During the last decade we have learned that the kidney pelvis heals fully as well as the kidney parenchyma if there is no obstacle to the outflow of urine. On the other hand he has found unexpectedly slow healing in a number of nephrotomy wounds. They have sometimes continued to discharge urine two or three weeks or more, even when there was no very evident obstruction to the outflow of urine. He does not recall, however, any slow healing pyelotomy wounds. During the past six months he has thrice opened the kidney parenchyma for the extraction of stone, and then deliberately inserted a probe into the kidney pelvis, and upon this opened the pelvis widely, inserted a rubber tube there for drainage, and closed the parenchyma by suture. Each one of these cases healed with the promptness characteristic of a pyelotomy. It seems, therefore, possible, not only that pyelotomy is to be preferred to nephrotomy for extraction of stone, etc., when this is possible, but that when nephrotomy is done it may seem wiser to suture the incision in the kidney parenchyma and to drain through a counter-incision made in the kidney pelvis.

Chemotherapy of Mercurial Compounds.—SCHAMBERG and KOLMER (*Am. Jour. Syph.*, 1917, i, 1) say that in the test-tube salvarsan exhibits a greater destructive influence on animal parasites, and mercury a greater destructive influence on vegetable parasites. Salvarsan is a powerful trypanocide and a feeble bactericide; mercury is a powerful bactericide and a relatively feeble trypanocide. Trypanosomes appear to react chemotherapeutically in a similar manner. Medicaments which have a destructive effect upon the former, likewise appear to exert a similar influence upon the latter. There is strong presumptive evidence that chemical substances which are capable of destroying trypanosomes in the animal body, exert a favorable influence in syphilis. Their laboratory experiments on trypanosomes and spirochetes point to a greater selective affinity of salvarsan for the Spirocheta pallida than is possessed by mercury. Mercuric chloride has a much greater organotropic effect than salvarsan; in their experiments mercury was fifty times more toxic for white rats than salvarsan. A group of new mercuric compounds has been prepared by them which far transcend mercuric chloride in their bactericidal power in the test-tube. One new compound has shown itself thirty times more powerful in this

respect, both by the Rideal-Walker and the "antiseptic" test. These new mercury compounds also exhibit a greater destructive influence upon trypanosomes than does mercuric chloride. Some of these compounds have shown a lower toxicity than mercuric chloride.

THERAPEUTICS

UNDER THE CHARGE OF

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The Relation of the Acid-base Equilibrium of the Body to Carbohydrate Metabolism and its Application in Human Diabetes.—UNDERHILL (*Jour. Am. Med. Assn.*, 1917, lxviii, 497) states that the ingestion of large doses of sodium bicarbonate has a marked influence in decreasing glycosuria in severe diabetes, and in maintaining the diabetic individual in a state of comparatively good health and vigor. This effect is ascribed to the neutralization of the exogenous and endogenous acid of the organism. In mild diabetes there is evidence that carbohydrate tolerance may be significantly increased by large doses. Finally, these conclusions are in harmony with experimental facts concerning the relation of acid-base equilibrium of the body to carbohydrate metabolism.

The Treatment of Pneumonia by Optochin.—CHESNEY (*New York Med. Jour.*, 1917, cv, 234) said that there was no doubt that ethyl hydrocuprein, or optochin, as it is known commercially, exerted a curative action in pneumonia. Optochin is a derivative of hydroquinone and was first demonstrated by Morgenroth and his co-workers, to have a specific inhibitatory action on pneumococci in the test-tube. Wright showed that the blood serum of patients who had received the drug was also bactericidal for pneumococci. In order to determine the time of appearance of the bactericidal action in the blood, specimens of blood were obtained from patients before and after the administration of optochin. The bactericidal activity of the serum was tested by the plate method upon actively growing cultures of pneumococci and the results showed that a bactericidal effect on the pneumococci was obtained if they were given an amount of the drug represented by 0.024 gram per kilogram of body weight for twenty-four hours. The time of appearance of the bactericidal action of the drug was shortened provided the first dose was relatively large and was followed at intervals of not more than three hours by smaller amounts. Thus, for an individual of average size the amount administered in twenty-four hours was 1.5 grams, and during the first twenty-four hours the best method of regulation was to give an initial dose of 0.45 gram following it at intervals of three hours by individual doses of 0.15 gram. During the second period of twenty-four hours the

drug could be given in 10 doses of 0.15 gram. It was best given in capsules. The hydrochloride was much more readily absorbed than the base and hence was to be preferred. The oral route of administration had been found to be more satisfactory than the intramuscular route, since the bactericidal action appeared in the patient's serum much more quickly when the drug was given by mouth. One drawback was the toxicity of the drug. These toxic symptoms are chiefly referable to the ear and eye. In all the cases of pneumonia treated with this drug and reported in the literature, one instance of permanent blindness had resulted and temporary impairment of vision in about 4 per cent. In a total of 786 cases reported in the literature the mortality was about 12 per cent. Leschke has emphasized the importance of beginning treatment early with optochin. He collected from the literature 204 cases treated within the first three days of illness with a result and mortality of 5 per cent., contrasted with 119 cases treated after the third day with a mortality of 21 per cent.

The Treatment of Iritis and other Eye Affections by Parenteral Injections of Protein.—MÜLLER and THANNER (*Med. Klin.*, 1916, xii, 1120) state that a number of different observers have reported beneficial affects following injections of foreign protein in the treatment of various acute and chronic affections. They report in this article their experience with such injections in the treatment of eye infections. They used for the injections 5 c.c. of fresh whole milk, boiled for four minutes. Four cases of parenchymatous keratitis due to inherited syphilis that had failed to yield to specific treatment showed marked inprovement after a single injection of the milk and continued to improve after subsequent injections. The most striking and prompt improvement was seen in 11 cases of iritis. In some of the cases the photophobia and pains disappeared within twenty-four hours and the inflammation subsided after a few injections. Those cases of iritis that were of gonorrheal origin did not show as prompt an improvement. They also describe the effects of the treatment in 9 cases of corneal opacity. The authors claim that the cornea became less opaque after the injections. No effect upon coroiditis, complicating corneal opacity, was noted. Because of its very favorable effect on 1 case of gonorrheal conjunctivitis of long standing they recommend that this treatment should be given a trial in every case of gonorrheal conjunctivitis in adults.

The Action of Digitalis in Pneumonia.—COHN and JAMIESON (*Jour. Exper. Med.*, 1917, xxv, 65) report a series of 105 cases of pneumonia studied by the electro-cardiogram simultaneously with digitalis medication. They found that digitalis given by the mouth has an action on the heart, because changes occurred in the auriculoventricular conduction time and in form of the T wave of the electrocardiogram, just as they do in the non-febrile heart. This conclusion is strengthened by finding that the pulse rate in fibrillating and fluttering cases feel in the presence of fever, exactly as it does in non-febrile cases. The dose and the time required to produce these effects are given and are the same as in the non-febrile cases. The authors conclude that digitalis acts during the febrile period of pneumonia. It produces a beneficial, possibly a life-saving effect in cases of auricular irregularity (fibrillation and flutter).

The Treatment of Diabetes Millitus by Prolonged Fasting.—CUMMIDGE (*The Practitioner*, 1916, xcvii, 414) holds the view that, while Allen's method is the best form of treatment at present available for cases of diabetes millitus of the acute or subacute types, it must not be concluded that it is an easy road to a cure, or that it can be used indiscriminately in all cases in which reducing substances are passed in the urine. Many cases of chronic glycosuria particularly in elderly people, do as well without, as with prolonged fasting, if the protein and carbohydrate of their diet is carefully adjusted to their metabolic capacity, and with much less discomfort to themselves; while cases of pseudolevulosuria improve more quickly when placed on a diet consisting of dextrinized starches and vegetables when there is mixed dextrosuria and pseudolevulosuria. An alternating diet gives good results but a preliminary fast is helpful in controlling the dextrosuria, and is advisable if dextrose is the prominent reducing substance in the urine. Before adopting the treatment by prolonged fasting, it is wise to make sure, therefore, that the patient will not benefit as much or more from some less trying method. The history of the case, the clinical condition, and the results of a complete analysis of the urine, collected for the second half of a forty-eight hour period, during which a test diet of known composition has been taken, controlled by several estimations of the sugar content of the blood and determinations of the alveolar carbon dioxide, should all be considered in arriving at a conclusion. If it is decided that Allen's method is likely to give the best results, it must be borne in mind that the fast is only a preliminary to the more difficult and delicate task of adjusting the diet to the patients defective powers of metabolism and promoting sufficient nourishment to keep him reasonably efficient and comfortable.

The Therapeutic Results of Parenteral Injections of Protein in Eye Affections.—FRIENLANDER (*Wien. klin. Wchnschr.*, 1916, xxix, 1329) reports 42 cases of severe trachoma treated by intramuscular injections of 10 c.c. of milk with marked beneficial effect. The interval between injections was never less than forty-eight hours, and in the more chronic cases that yielded stubbornly to the treatment the injections were four days apart. The injection was almost invariably followed by a chill and sharp rise of temperature, and the succeeding injection was not given until the entire subsidence of this reaction. He reports in detail a few of the typical cases treated on this plan and is convinced that the epidemic of trachoma was promptly checked by the injections.

Diagnosis and Clinical Characteristics of Gout.—PRATT (*Boston Med. and Surg. Jour.*, 1916, clxxv, 925) says that the prompt relief from pain produced by colchicum in gout is so striking that many have asserted that this drug is as specific in gout. It is certainly an aid in diagnosis, as colchicum does not have such a marked effect in relieving the pain in acute rheumatism or in other conditions which may be confounded with gout. Salicylates rarely have any marked effect in controlling the pain of acute gout. The relief from the severe pain of gout by atophan is even more striking than that produced by colchicum. Its value in diagnosis is probably less, as it often is of considerable aid in checking the pains of non-gouty arthritis.

OBSTETRICS

UNDER THE CHARGE OF

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Acidosis in Normal Pregnancy.—EMGE (*Am. Jour. Obst.*, November, 1916) has studied 68 cases of normal pregnancy to determine the presence or absence of acidosis. By a chemical method he endeavored to ascertain the carbon dioxid in the blood plasma. The results showed that out of 61 cases 55 had acidosis. In practically all of the cases there was acidosis to some extent, but the degree varied so that in some it was scarcely appreciable. An effort was made to ascertain what causes this condition. It was thought that multiple pregnancy might be responsible, but this could not be proved, nor was the period of pregnancy responsible for the condition, because it was found equally in the first and last weeks. In those patients who retained little food it was not especially frequent. In one case where the patient starved herself there was a marked diminution in the carbon dioxid tension in the blood plasma. In one non-pregnant woman, just preceding menstruation, there was a lessened tension but this became normal or above normal later on. Out of 61 cases of pregnancy only 2 did not show a decrease in carbon-dioxid tension indicating acidosis; one of these was a chronic alcoholic who gave birth to a seven months macerated fetus two weeks before term. In the puerperal state 25 patients were studied. In nineteen the condition of acidosis had disappeared; 1 patient had chronic interstitial nephritis, and the findings did not become normal in this case. The remaining 5 did not regain the normal standard but showed little variation. One patient had preeclamptic toxemia when her blood plasma showed a marked diminution in carbon dioxid tension. Labor was induced. Two normal cases were examined during labor and they showed low gas tension and moderate carbon dioxid deficiency. These and similar studies show that acidosis is present in the great majority of pregnancies in varying degree. Where, however, a marked diminution from the normal is present, the finding is significant and adds to the factors from which an estimate of the gravity of the patient's condition can be made.

The Umbilical Cord and its Complications as a Cause of Infant Mortality.—YOUNG (*Am. Jour. Obst.*, November, 1916) reports the case of a primipara with normal pelvis who had previously a laparotomy for septic peritonitis. The membranes ruptured prematurely and the effort was made to dilate the cervix by inserting a bag. When full dilatation had been obtained pituitrin was given; the head engaged and was observed to markedly recede between the pains while the patient suffered considerably from shock. The occiput was obliquely anterior on the right side. The application of the forceps failed and an axis traction, with the services of an assistant, making traction on the bar of the forceps, succeeded in delivering the child. The patient was markedly shocked during the delivery. On examination the cord was three times about the child's neck and had been tightly pulled by the

delivery. The child was dead. The placenta was on the posterior aspect of the uterus near the fundus. Measurements showed that from the umbilicus to the placental origin there was but 9.5 cm. of umbilical cord. In discussing this paper before the New York Academy of Medicine it was remarked that such complications were not infrequent after the use of pituitrin and that the infant was often born asphyxiated. Shortness of the cord is comparatively rare and when one is less than 50 cm. in length it must be considered abnormal. Cords as short as 37 cm. have been observed. In some cases of short cords violent expulsive pains may deliver the child tearing off the cord at the umbilicus. Hemorrhage may then be controlled by a circular purse-string suture, grasping the vessels and closing over the torn end of the cord. If considerable coiling of the cord can be diagnosed so that delivery through the vagina will result in the death of the child, the indication is clear for Cesarean section. It may be added that the coiling of the cord about the child may prevent a natural onset of labor. In a case under the observation of the reviewer a weak primipara went full term without signs of labor; the phenomena of descent and engagement absolutely failed, and elective section was performed. The cord was found coiled three times about the neck, across the chest, and under the axilla. The delivery of a living child through the vagina would have been impossible. In diagnosing the coiling of the cord about the fetus, a hissing sound faster than the placental bruit, and slower than the fetal heart sound, is strongly suggestive of this complication. When the fetus can be mapped out by palpation a stethoscope placed over the fetal neck may elicit this sound.

Toxemia in Pregnancy after Thyroidectomy.—Kosmak (*Am. Jour. Obst.*, November, 1916) reports the case of a patient upon whom thyroidectomy had been done who was in the pregnant condition. There had been marked nausea and vomiting, with constipation, attacks of nervousness, flushes, and tachycardia. The pulse was small in quality and about 110. The abdominal tumor was that of a five months' pregnant uterus. The patient continued under observation, but a great deal of difficulty was experienced in correcting the nausea and vomiting, and there was much neuralgic pain. These symptoms continued, although the urine was practically normal. With the hope of improvement thyroid extract was given in small doses, but apparently without effect. The condition of toxemia became so pronounced that several weeks before full term an attempt was made to induce labor by introducing the Vorrhees bags. This failed and although the membranes were ruptured and amniotic liquid allowed to escape, labor did not develop. An extraperitoneal section was then done, and just preceding the operation pituitrin was given. When the uterus was incised it was found to be in a state of tonic contraction and the delivery of the fetus was so different that a stillbirth resulted. The patient made a fairly good recovery although there was sloughing in a portion of the abdominal wound. About three weeks after labor the patient's toxemic condition became worse and nephritis developed. On referring to the patient's surgical history it was found that the case was one of adenoma of the thyroid, and the surgeon left what he believed was sufficient of the gland substances to carry on the gland function. The right lobe and the anterior half of the left lobe were removed.

GYNECOLOGY

UNDER THE CHARGE OF

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Imperforate Hymen Causing Symptoms in a Child.—An interesting and rather unusual case of the occurrence of marked obstructive symptoms, due to imperforate hymen, before the onset of menstruation is reported by WIENER (*Am. Jour. Obst.*, 1917, lxxv, 398). The patient was a girl of twelve, admitted to the hospital complaining of difficult micturition and enlargement of the abdomen. She had had to be catheterized a number of times before coming to hospital. On examination, the hymen was found to be imperforate and bulging; there was a median hypogastric mass reaching up to the umbilicus, fluctuating, but not tender. This mass was not reduced in size on emptying the bladder. The preoperative diagnosis was naturally hematocolpos, but on excising the hymen about 30 ounces of thin, yellowish-white turbid fluid was evacuated. The vagina was enormously dilated, with an infantile uterus at its summit. The origin of the fluid was apparently the glands of the endometrium and cervix, which for some reason had been unduly active.

Relation between the Age of the Ovum and Sex.—During ordinary conditions of life it is practically impossible to determine in any large series of cases the exact date of conception, and therefore to determine at what period in the life-history of the ovum it has become fertilized. In war times, however, this becomes comparatively easy, owing to the fact that soldiers are allowed home on leave for a few days at comparatively long intervals, and the time of fruitful intercourse can therefore in many instances be determined with a fair degree of accuracy. A very interesting series of observations upon this point have been reported by SIEGEL (*München. med. Wchnschr.*, 1916, lxiii, 1787), who thinks there is a very definite relationship between the age of the ovum when fertilization takes place and the sex of the resulting individual, fertilization of young ova resulting in the production of females, of more mature ova in the production of males. If we assume, he says, as has been pretty conclusively demonstrated, that ovulation commonly occurs between the tenth and fifteenth day after the beginning of the preceding menstruation, we may consider the ovum as *young* from about the eleventh to the twenty-third day of the menstrual cycle (counting always from the first day of the period); as maturing from the twenty-fourth to the twenty-sixth day, and as *mature* or "überreif" from the twenty-sixth to the ninth day. In a tabulated series of 115 cases in which time the conception could be determined, Siegel found that of conceptions occurring from the twenty-seventh to the ninth day of the menstrual cycle, *i. e.*, resulting in the fertilization of a mature ovum, there were born fifty-two boys and eight girls; of conceptions occurring from the tenth to the fourteenth day, resulting in the fertiliza-

tion of the young ovum of that cycle or of the mature one of the preceding cycle, there were born ten boys and fourteen girls; of conceptions occurring from the fifteenth to the twenty-third day, resulting in the fertilization of young ova, there were born five boys and twenty-six girls. In other words, conception occurring with mature ova resulted in 86 per cent. of boys; with young ova in 84 per cent. of girls, and those occurring at the intermediate period in about an equal division of the sexes. A smaller series of 25 cases, observed by another author and quoted by Siegel, give practically parallel results. These findings are quite in accord, says the author, with facts demonstrated by animal experiments, and well known to breeders of dogs and cattle, who make use of them in the development of their stock.

Chronic Urethral Gonorrhea in the Female.—The great importance of this condition, and the fact that it is frequently overlooked or regarded too lightly, is emphasized in a recent article by BIZARD and BLUM (*Presse méd.*, 1917, p. 46). They point out that it affects chiefly young girls and nulliparæ, infection of the cervix being more common in parous women. It exists in two chief forms: Primary ("l'urétrite chronique d'emblée"): This is not very rare; it manifests itself as a pure urethritis, without other localization of gonococci. It is absolutely symptomless, producing no pain, burning, or abnormal sensation, but a drop of thick pus containing masses of gonococci can be expressed from the urethra. Unless a drop of this pus happens to be present at the meatus at the time of examination, however, the only visible evidence of the condition will be a slight puffiness of the tissues. The course of the affection is protracted; it remains torpid, the gonococcus is very tenacious, and treatment is apt to be required for weeks or months. Secondary: This is even more frequent than the primary form; it is found in women cured of a primary vulvovaginal gonorrhea. It manifests itself as a very slight urethral discharge, coming on two or three months after other condition, and rarely sufficient in amount to stain the clothing. Occasionally this form is painful; and sometimes the discharge is sufficiently profuse to be troublesome to the patient. The characteristic sign is, again, the drop of pus, often secured by the physician only after considerable trouble. The patient must be examined before micturition, and often early in the morning, before the first micturition of the day. In cases where the condition is very chronic, and the deeper portion of the urethra is affected, vigorous and prolonged massage of the latter, starting at its inner extremity and pressing it vigorously up against the pubis, is necessary to bring a drop of pus to the meatus. It may even be necessary to scrape out some epithelial elements from the urethra by means of the platinum loop in order to get material for study. The treatment of urethral gonorrhea in women must be persisted in for a long time, and must be mild. It consists in three chief methods: massage, lavage, and applications. Massage is to be done gently, with the finger inserted deeply into the vagina, always from behind forward, care being taken not to injure the urethra against the pubis. Lavage may be done either with or without a catheter, using potassium permanganate 2.5 per cent., oxycyanide of mercury 1 to 1000, or copper sulphate 2 to 1000. Applications must be made every day, but very gently and cautiously. The

mucosa should never be made to bleed, and the treatment should cause no pain after the patient has become accustomed to it. An oily fluid is used such as pure icthyol or gomenol, applied with a cotton-tipped applicator. After apparently cured, the patient should be reëxamined at regular intervals to detect any possible recurrence.

OTOLOGY

UNDER THE CHARGE OF

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War-deafness.—LERMOYEZ (*Monde méd.*, January 17, 1917) in this paper limits his observation to the impairment of hearing due to direct and indirect trauma, the former including immediate injuries to the temporal bone and the latter being limited to the effect of concussive shock upon the perceptive apparatus. Immediate trauma is that which is inflicted directly upon the temporal bone, mediate trauma is an injury to the auditory apparatus consequent upon a damage to the cranium and includes the effect of contusions and blows upon the head, a considerable decrease in hearing or complete deafness, resulting with, or without, fracture of the skull. Under the eventualities of modern war conditions in immediate trauma there is usually the penetration of projectiles or bullets or pieces of shell into the temporal bone and these, so far as procedure is concerned, may be divided into two classes, those in which the projectile is visible at the fundus of the external auditory canal permitting immediate removal, and those in which the penetration is deeper with invasion of the petrous portion of the temporal bone or beyond, in which surgical intervention may be made to follow upon the sequence localizing events, surgical intervention following the evidence of a suppurative discharge from the ear, facial paralysis, labyrinthine or meningeal phenomena. In transverse fracture of the petrous portion of the temporal bone, in the great majority of cases, the lesion is perpendicular to the axis of the bone extending from the posterior to the anterior foramen, involving the vestibule and cochlea, but sparing the middle ear; the organ of Corti is usually destroyed and the auditory and facial nerves may be lacerated or divided and there is, usually, a free persistent discharge of cerebrospinal fluid with concomitant signs of fracture of the skull. The impairment of hearing is usually unilateral, and on the recovery of consciousness after the injury there is usually high-pitched tinitis in the affected ear, dizziness, nausea and static disturbance, the latter symptom being sometimes reliable by lumbar puncture. In the longitudinal injury of the temporal bone the temporal parietal region is especially involved and the line of fracture usually runs parallel to the axis of the petrous bone, opening the tympanic cavity, but not necessarily involving the internal ear except as the result of concussion,

the drum-head is usually ruptured and the roof of the tympanum sometimes fractured. The symptoms vary in these cases from those occurring in transverse fracture, there is free, intermittent and prolonged otorrhagia, the impairment of hearing, at first decided, is frequently fugitive and there is rarely dizziness and facial paralysis, and the danger attending this type of fracture is less immediate to the injury itself than to the effect of subsequent infection and the extension of a suppurative process; the hearing is, as a rule, not irremediably lost unless this may come about later as a sequence of the suppurative process. The first aid dressing as recommended by the author is that of dry cleansing and the plugging of the auditory meatus with iodoform gauze, lavage of any kind being contra-indicated. The consequences of indirect trauma constitute in the opinion of the author the true war deafness. With the approximate bursting of a shell the auditory perception disappears without injury to the petrous bone and without evidnece of cranial impact. In some cases the intensity of the noise partly inhibits the auditory nerve or the actual aërial concussion results in such movements to the labyrinth, as to result in serious lesion in that organ. In actual experience there would seem to be two types of this form of labyrinthine concussion, one mild and the other severe. In the mild form the patient is stunned from the shock of the explosion, there is no pain, he can hear musical sounds, and there is no discharge from the ear. The condition improves in the course of a few days or weeks, under conditions of rest, without treatment and the patient is able to return to duty. In the cases of severe concussion the subject often loses consciousness, on recovery he is often unable to stand, is nauseated, he has variable vertigo, increased by movement of the head or the sight of moving objects; his injury is a major one and he must be transferred to a base hospital. The drum-head under these conditions is sometimes found to be the seat of hemorrhagic spots which suggest the possibility of similar lesions in the labyrinth. The future of the hearing is uncertain and the prognosis in that respect must necessarily be guarded; usually the subjective noises and the vertigo gradually decrease and equilibrium is restored except in the event of sudden movement, while the impairment of hearing, at first partial, gradually becomes more decided. In the great majority of the cases local treatment is advisedly limited to the removal of the foreign objects and such repair of the impacted tissues as may be necessary, dry treatment being usually preferable to moist, antiseptic solutions being usually contra-indicated, it being the opinion of the author that the aurist may be more dangerous than the enemy in the event of his incautious intrusion. A due consideration of the element of time in the determination of the extent of the injury effected by concussion of the auditory apparatus which is urged by the author, is seconded by E. J. Mowre and Piatri in their essay entitled "The Auditory Organ in War Time," published in the *Arch. de méd. et de pharm. militaries*, in the first part of which, entitled Labyrinthism, the authors lay stress upon the necessity of care in the physical and functional examination of the subjects and in that accuracy in recording the history and especially the circumstances of the original causation, which mark the work of the history-taking as done in the French war hospitals, repeated examination, static and auditory, being advocated

as necessary and indispensable for the detection of conscious or unconscious aggravations by the patients or else supplementary to possible omission in early investigations, the expert otologist finding that, in case of an injury to the ear, the importance of the blow or of the shell shock bears an indirect relation often to the auditory and static disorders. Undue precipitancy in diagnosis is deprecated, and a review of each case in six months or a year for a definite opinion is insisted upon.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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Studies on Experimental Scurvy in Guinea-pigs. — JACKSON and MOORE (*Jour. Infect. Dis.*, September, 1916, xix, No. 3) studied the occurrence of a peculiar infection in a number of guinea-pigs in the laboratory of St. Luke's Hospital, Chicago, concerning the effect of milk diets on guinea-pigs. The animals appeared partially paralyzed and the muscles and knee-joints were swollen and tender. The diet in addition to green food and water consisted largely of milk from a cow having experimental streptococcal mastitis. Experiments were carried out to determine what factors in the diet were responsible for the condition. Groups of animals were fed on various combinations of food chiefly in relation to milk or milk constituents to test both the production of the disease and its prevention. Experimental scurvy was produced in guinea-pigs by diets of pasteurized, raw, boiled, skimmed and condensed milk, streptococcus broth and milk, milk and green vegetables, thyroid extract and milk, casein and water, oats, and bread and bran. Scurvy was not prevented by adding calcium lactate to milk or injecting it into guinea-pigs on a milk diet, nor did the injection of olive oil have any effect in preventing scurvy in these animals. Those pigs fed on a diet of cream, or of olive oil added to milk, showed a "fat constipation" from the effects of which they soon died. Milk-broth cultures of Streptococcus viridans and Streptococcus hemolyticus, water, lactose water, lime water and goat's milk did not produce typical scurvy in the animals whose diet they comprised. Guinea-pigs living on a milk diet showed, as clinical symptoms, preliminary loss of weight, swelling of the joints, and occasionally hyperemia of the gums. Fractures of the long bones near the epiphyseal ends and deformities were commonly observed. The most important pathological lesions noted at postmortem examinations were hemorrhages, found in the

muscles, bone marrow, tooth pulp, costochondral junctions and sometimes in the skin and lymph glands, enlargements of the ends of the long bones and swollen lymph glands. Microscopically the earliest lesions which were seen were a slight necrosis and hemorrhage in which coccus-like bodies were frequently observed. The only evidence of inflammation is slight fibrin foundation and the presence of numbers of mononuclear and polymorphonuclear eosinophile cells. The average time for the onset of symptoms with the pasteurized milk diet was nineteen days; with other diets from eleven to nineteen days. The earliest lesion was observed on the tenth, the latest on the twenty-ninth day. The disease was afebrile and produced no great increase in leukocytes. Cultures of the heart's blood from guinea-pigs with scurvy from milk diet were sterile and passage of blood from these animals to normal animals did not produce the disease in the latter.

Trench Fever.—HURST (*Lancet*, October 14, 1916, cxci, No. 4859) states that among the cases of fever occurring in the British armies in France and Salonica, a considerable number existed in which the diagnosis was doubtful and which were designated as pyrexia of unknown origin. In the early summer of 1915, a number of cases of fever in which two periods of pyrexia were separated by a normal interval were recognized and called trench fever. Later, other investigators described cases of the same disease and showed that there are two distinct clinical types of it. The cases only occurred among officers and men living near the trenches and in the personnel of hospitals and it was for this reason that the name "trench fever" was given to it, although actual residence in the trenches was not an essential factor. Many cases of the first type occurred in the armies in France and Flanders early in 1915 and later in the same year, many cases of the second type occurred. Since December, 1915, the disease has also been very prevalent in Salonica where the infection was probably brought from France. Although trench fever resembles paratyphoid fever during the first pyrexial period, although it is of a characteristic relapsing type and although it may simulate malaria in the short sharp attacks, yet blood taken at different periods has always been sterile, the Widal reaction has always been consistently negative and no spirochete or malarial plasmodium has been found in blood films taken during febrile and afebrile periods. McNee and Renshaw found that trench fever could be transmitted to healthy men by intramuscular or intravenous injection of the blood of patients with the disease. The red corpuscles have the same effect but not the plasma and serum. One attack does not protect against reinfection. No fatal cases have occurred so the true nature of the disease remain unknown, although the striking periodic character of the fever, the considerable increase in proportion of large mononuclear leukocytes and the evidence of an intracorpuscular infection suggest a protozoal origin. All the evidence collected as to the method of propagation seems to point to the fact that the disease is conveyed by lice; cold wet and fatigue seem to be exciting causes in a man who has become infected but shows no symptoms. The author states that as the result of his observations he has concluded that the incubation period is from fifteen to twenty-five days. The disease usually begins without any premonitory symptoms

except a feeling of malaise. The patient complains of severe headache, backache and pains in the legs, shivers and often sweats profusely. The onset is sometimes very abrupt; the patient is giddy, shivers and may be very short of breath. He has a pain in his left side and pain and tenderness in the legs, especially in the shins. Leukocytosis is often present and the percentage of hemoglobin is generally about 80 though the number of red corpuscles is undiminished. In the short form of trench fever, the temperature rises rapidly to between 102° and 104° F. and on the third or fourth day suddenly falls. The pulse rate is only slightly increased. In the long or periodic type, the temperature rises to between 101° and 104° F. on the first evening, and the pulse is usually accelerated in proportion with the temperature. This initial attack is variable in duration. All the symptoms disappear with the fall of temperature at the end of the initial attack and the patient is well for from two to ten days. Then the general symptoms reappear although not in so severe a form. Recurrence follows periodically, the maximum temperature always being reached in the evening. The diagnosis can only be made with certainty from a study of the temperature chart but the association of pyrexia with tender shins is very suggestive of trench fever. The possibility of malaria and relapsing fever should be excluded in making the diagnosis. No fatal cases of trench fever have occurred and the patient never seems seriously ill, except occasionally for a short time in the first attack. The total duration of the periodic type of trench fever from the onset to the end of the last attack is usually between four and six weeks. As the disease is probably conveyed by lice, which become infected by biting a patient during an attack, efforts should be made to keep troops free from them. All cases of trench fever should be isolated and the patients' bedding and clothes thoroughly disinfected. No treatment has been found which prevents the periodic return of attacks or which is really effective in overcoming the pain although some relief may be obtained if constipation is prevented by aperients, and hot applications are used for the pain.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Experimental Cloudy Swelling of the Kidney in Rabbits.—The term cloudy swelling is a most indefinite one to the pathologist. As it was originally applied by Virchow the term indicated a swelling and tur-

bidity of a tissue to be recognized in the gross. This appearance has been accepted by the majority of pathologists as an evidence of intracellular change impeding the normal function of the cells. It was subsequently found that certain characteristic changes could be recognized microscopically which were also spoken of as cloudy swelling. Some discrepancy, however, was found in that the naked-eye appearance of cloudy swelling did not always demonstrate the same microscopic picture. The older authors claimed that more reliance could be placed upon the naked-eye characters than the presence of minute cellular change. It is true that autopsy material from human cases does not permit parallel conclusions by the macroscopic and microscopic method. The swelling which is often observed in tissues is not the result of a common cause and the cloudiness is so variable in its character than an agreement in diagnosis is rarely found among different observers. SHANNON (*Jour. Lab. and Clin. Med.*, 1916, i, 541) studied cloudy swelling in rabbits. By various means, removal of the kidney, ligation of ureter, injection of tartaric acid, liver substance, and bacteria, he brought about various changes in the kidney simulating cloudy swelling. He observed that under normal conditions the cells of the kidney tubules contained numerous albuminous granules, which could be stained by various methods and were caused to disappear by the application of alkalies. By the removal of one kidney these granules became more prominent in many of the tubules of the remaining organ. Although the microscopic granulation was thus intensified, the gross appearance was but little altered. On the other hand the injection of tartrates led to a markedly swollen and cloudy kidney in which no increase of albuminous granules could be observed. Intraperitoneal injections of autolysed liver produced a markedly cloudy swelling with the disappearance of the microscopic granules. Under the conditions in which a gross swelling and cloudiness of the organ made its appearance in the absence of a granular deposit in the cells, the process appeared to be the result of edema and tissue disintegration. Acute toxemias led to a disappearance of the normal granules, while suppurative processes attended with emaciation caused an enormous increase in swollen cells. The author found that kidneys with much increase of albuminous granules usually gave a normal phthalein output. This form of cloudy swelling is claimed to be a physiological response to an increase of protein waste products of the blood and not a degenerative change.

Anatomical Lesions in Late Acquired Syphilis.—The wide-spread distribution of syphilis has led to the advice that, when in doubt in diagnosis suspect syphilis. This suggestion prior to the days of the Wassermann reaction had its value but is no longer as forceful. Some discrepancy still exists between the clinical findings and the observations at autopsy in that a certain number of cases do not demonstrate recognizable anatomical lesions even where a positive Wassermann has been obtained. The reverse is also true. SYMMERS (*Jour. Am. Med. Assn.*, 1916, lxvi, 1457) has given an excellent analysis of almost 5000 autopsies performed at the Bellevue Hospital. Of this number 314 cases of syphilis were found. Many interesting points were brought out in this analysis indicating the incidence and distribution of anatomical lesions in acquired syphilis. Evidences of skin infection were

observed 106 times. This figure indicates the frequency of residua of the secondary rash. Lymphoid hyperplasia was only observed in 20 cases, indicating the transient character of the disease in this tissue unless succeeded by interstitial fibrosis. Syphilitic lesions of the caseous system were encountered 48 times, the majority of them involving the bones of the head. The tibia was affected 16 times. The presence of syphilitic processes in the testis is commented upon by the author. Among 171 males interstitial orchitis was found 67 times. In no case was gumma of the testis found. The latter, it is stated, is an unusual syphilitic process, the author having never met with the lesions in several thousand autopsies and but once in a surgical specimen. A characteristic syphilitic lesion of the base of the tongue is emphasized. This lesion consists of an obliteration of the normal surface markings and smoothness and induration of the surrounding tissue. It is spoken of as the smooth or indurative atrophy of Virchow. In a particular series of 623 autopsies acquired syphilis was determined in 75 instances and of this number 85 per cent. presented signs of indurative atrophy of the base of the tongue. In the present series of 314 cases of late acquired syphilis it was recorded in 25 per cent. Lesions of the respiratory tract occurred 35 times. Of these the larynx was involved in 12, the lungs in 12, and the trachea in 4 cases. Evidence of syphilis of the nervous system was observed in 112 of the 314 cases. The liver also was a favorite site for lues, showing its presence 105 times. Hepar lobatum occurred 50 times, the majority of cases occurring between the ages of twenty and fifty. Associated with the liver changes the spleen was enlarged in 32; jaundice was present in 14 and ascites in 11. The highest incidence of the localization of the syphilitic process was observed in the aorta. There were 175 cases of aortitis; or nearly 56 per cent. The arch of the aorta was involved 109 times and in 42 cases the entire vessel was diseased. The combination of thoracic and abdominal aortitis was present 3 times. Aneurysmal dilatation of the aorta was observed 39 times and saccular aneurysm 45 times. The majority of these concerned the arch. In 1 case as many as 8 aneurysms were found in the vessel. The aortic valves were sclerosed in 64 instances, and definitely retracted in 27. In 51 of the 175 cases of syphilitis aortitis the lesion in the aorta was the only manifestation of syphilis. It is also interesting that syphilitic aortitis is not uncommonly associated with lesions in the coronary arteries. This was observed 45 times. Gastric ulcer of syphilitic origin was observed once. The literature contains only 12 other examples of a similar nature. Luetic lesions of the intestine in which ulceration or stenosis was present, was found in 6 subjects. In the entire series of 314 cases of organic syphilis, gummata occurred 65 times. The majority of these were in the liver.

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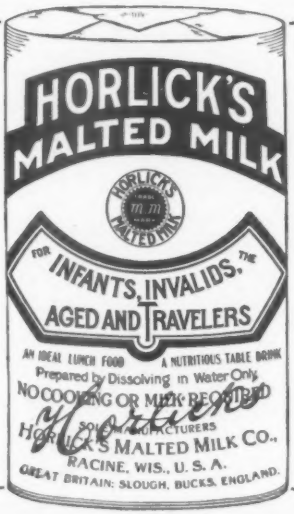
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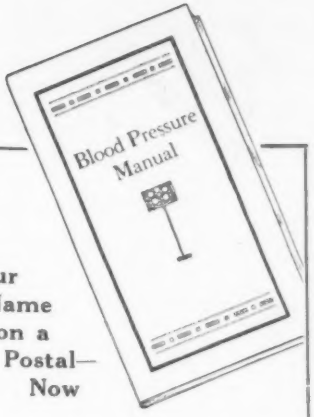

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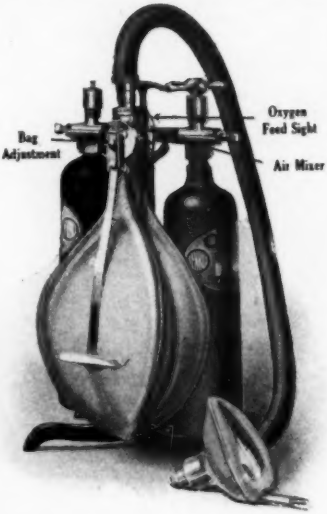

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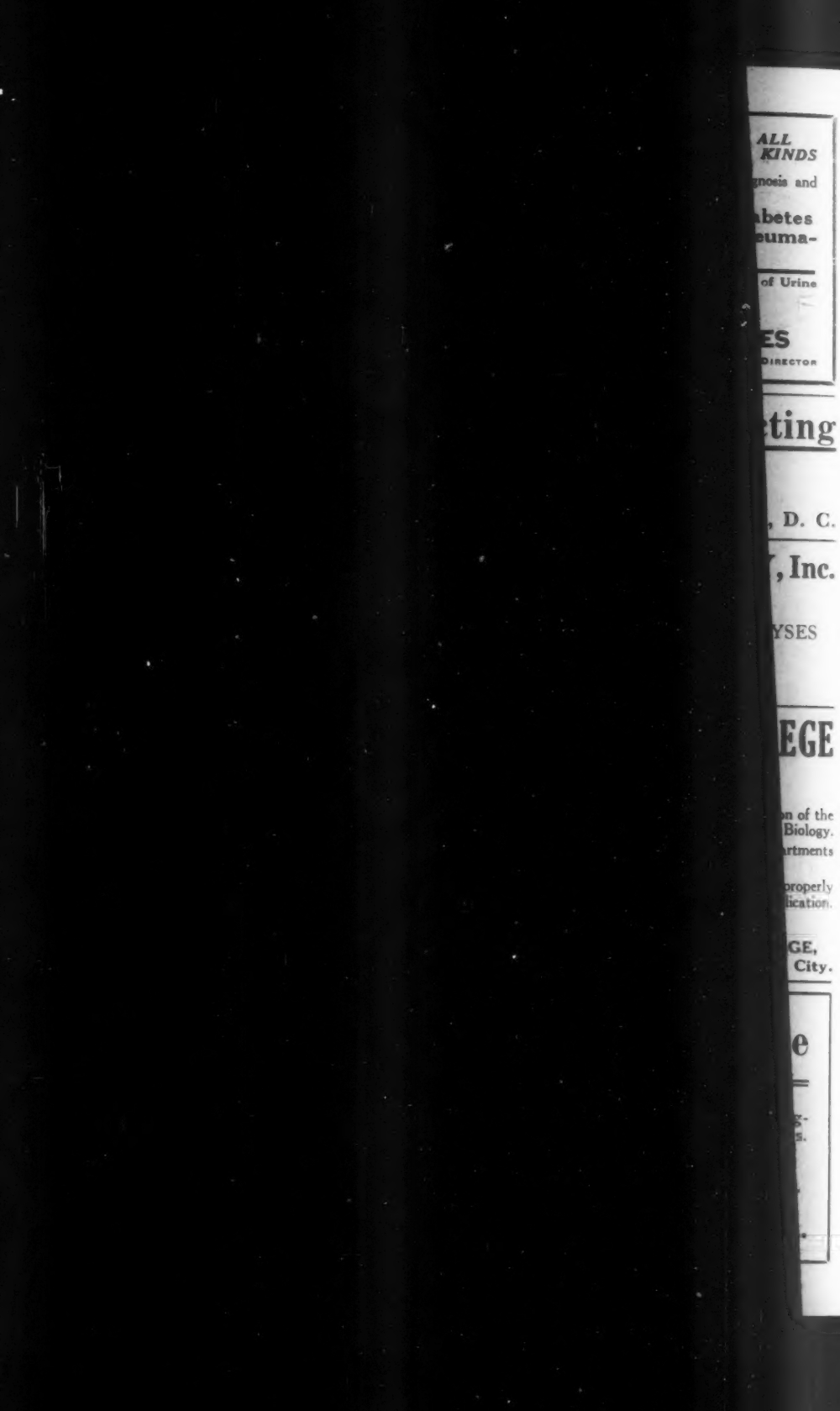

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